November 2010 Issue 4

FETAL ALCOHOL FORUM©

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The International Medical e-Network devoted to Fetal Alcohol Spectrum Disorders

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Issue 4 – November 2010

INTRODUCTION


Susan Fleisher

In our Fourth Issue we are honoured to have original articles contributed by four diverse FASD experts:

- **Kenneth R. Warren, Ph.D,** the Acting Director of the National Institute on Alcohol Abuse and Alcoholism and National Institutes of Health, USA
- **Dr Kathleen Sulik,** Professor, the Department of Cell and Developmental Biology and the Bowles Center for Alcohol Studies, USA
- **Kathryn Kelly,** Project Director of the FAS/E Legal Issues Resource Center and Fetal Alcohol and Drug Unit in Seattle, Washington, USA
- **Paula Abate, Ph.D.** Associate Researcher Laboratory of Alcohol, Ontogeny and Learning, Instituto de Investigación Médica Mercedes y Martín Ferreyra, Córdoba, Argentina.

In response to the recent debate, we have created the section, LOW LEVEL STUDIES FROM AUSTRALIA AND BRITAIN. You can read the studies, some of the press that triggered the debate and thought provoking responses from our FASD experts.

For the first time we have an enquiring "Letter to the Editor" from Dr. Guy Ratcliffe, the recently retired Director of the Medical Council on Alcohol.

Since our last issue we have noticed an increase in FASD research around the world. You will find abstracts of 120 new studies published during the past six months.

Our FASD world seems smaller and closer as we receive weekly requests from doctors and researchers around the world asking to be added to our mailing list. Please continue to download the FETAL ALCOHOL FORUM from our website: www.nofas-uk.org, share it with your colleagues and send us your articles and feedback. To join the FORUM network, click here.

It is our hope that the FETAL ALCOHOL FORUM will grow the fetal alcohol research network and ultimately help us all to reduce fetal alcohol harm.

Susan Fleisher
Publisher

Vandana Alimchandani
Editor/ Technical Support Supervisor

Elizabeth Mitchell
Associate Editor

DEDICATION

Professor Martin Plant
1946-2010

Martin Plant had a passion for mountaineering

We dedicate Issue 4 of the FETAL ALCOHOL FORUM to Professor Martin Plant, one of the world's leading experts on alcohol and addiction. Professor Plant was renowned for his research in the alcohol field with his wife Professor Moira Plant.

NOFAS-UK is indebted to Professors Martin and Moira Plant for their support and contributions over the years, including their article in Issue 2 of the FETAL ALCOHOL FORUM, *Alcohol and Women in the United Kingdom: What's Happening?*

Professor Plant dedicated his career to drug and alcohol research and improving the lives of those who were disadvantaged. He was Director of Alcohol Research in Edinburgh's Department of Psychiatry (1978-97) and the Director of the Alcohol and Health Research Centre. In 2002 he moved to Bristol to become Professor of Addiction Studies at the University of the West of England where he collaborated with his wife Moira.

Professor Plant published countless studies and books, such as *Drinking Careers* (1979), *Drugs in Perspective* (1981, revised 1987) and a novel, *Project Wolf* (2000) about Wolves in Scotland, *Binge Britain: Alcohol and the National Response* (2006) co-authored with his wife Moira and his last book, *Drug Nation* (2010).

Professor Plant died of heart failure on 16 March 2010 and is survived by his wife and daughter Emma.

Professor Plant was a gifted gentle giant and a powerful positive force in the lives of all those of us who knew him. He made the world a better place and will be missed by many.

Susan Fleisher
NOFAS-UK

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LETTER TO THE EDITOR

ABSENCE OF ROBUST DATA PREVENTS CLARITY OF INCIDENCE OF FASD IN UK

Greater awareness in the population of the impact of alcohol on the unborn foetus is a welcome development, whereas the resulting abnormalities are anything but. Whether the full-blown foetal alcohol syndrome is the result or some of the associated affects, the consequences for child, parents and carers may be little short of catastrophic. Parents frequently feel guilty whenever a baby is born with some congenital defect. Could this abnormality have been prevented? With regard to alcohol the answer is unquestionably 'yes'.

In my time with the Medical Council on Alcohol expectant mothers would ring expressing concerns that they had consumed alcohol following conception but before pregnancy, planned or unplanned, was confirmed. Reassurance at such times is paramount, as well as common sense advice to avoid most if not all alcohol for the duration of their pregnancy. The safest practice of course remains total abstinence once the pregnancy is confirmed. Inevitably some women requested advice about possible termination. Advice to discuss this issue with their obstetrician was given routinely.

Nevertheless one outstanding anomaly exists within the UK about FASD. No robust data exist defining its incidence: attempts to establish research projects have failed primarily due to a lack of funding. This has resulted in merely estimating the figures based primarily on data from abroad. Surely it is incumbent on those involved in managing the physical problems as well as the difficult behavioural problems in afflicted children, as well as the psychological problems in the families rearing these children, to be able to specify accurate risk assessments based on current UK data. Incidence of FASD can potentially be reduced to nil, but surely we should have a clearly defined start point from which to initiate the required downward spiral.

Dr Guy Ratcliffe

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ORIGINAL ARTICLES BY FASD EXPERTS

I. TWO FORTY YEAR ANNIVERSARIES: THE RECOGNITION OF FAS AND THE ESTABLISHMENT OF THE NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM

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The year 2010 marks the 40th anniversary of the National Institute on Alcohol Abuse and Alcoholism (NIAAA), one of the 27 Institutes and Centers that currently comprise the National Institutes of Health (NIH) in the United States. By coincidence this year also marks the 40th anniversary of the initial clinical recognition in the U.S. of the effects of prenatal alcohol consumption on the developing fetus (Ulleland, 1970). Paul Lemoine's observations of prenatal alcohol effects in France, published two years earlier (Lemoine, et al 1968), had failed to attract any attention in the U.S., or Europe for that matter. It is no coincidence, however, that much of our understanding of what we now call fetal alcohol syndrome (FAS) and fetal alcohol spectrum disorders (FASD) has accrued because of the existence of NIAAA over the past 40 years. From its earliest days, NIAAA has invested heavily in FASD research and prevention, and has led efforts to bring public attention to this major public health problem.

Dr. Christy Ulleland's initial U.S. report of fetal alcohol effects in 1970 was followed in 1973 by two publications in Lancet, by Dr. Ulleland and Drs. Kenneth Lyons Jones and David Smith (Jones, Smith, and Ulleland 1973; Jones and Smith 1973). These events were reviewed by Dr. Jones in this newsletter (issue 1, May 2009). Also in 1973, NIAAA began to fund research on FAS. NIAAA's first research grants were awarded to study the fetal effects of alcohol in rodents and other animal models. Three clinical investigations, to follow pregnancy outcomes among women who consumed alcohol in pregnancy, were also begun at that time. One of these, the Pregnancy and Health Study, undertaken by Dr. Ann Streissguth, became a long-term follow-up study nicknamed the "Seattle 500", and has continued to follow children born in the study for more than 30 years. Funding for another pregnancy outcome study was awarded to Dr. Jan Kuzma at Loma Linda University. Funding for the third of these early studies was awarded to Dr. Joel Alpert at Boston City Hospital along with Dr. Hank Rossett, a psychiatrist from Boston University and an early NIAAA Career Teacher. Both Drs. Streissguth and Rossett became major leaders in the FAS research and prevention communities.

When I joined the NIAAA in 1976, one of my first responsibilities was to organize the first national meeting on FAS research, where research findings from animal and human investigations were to be presented. The meeting occurred in February of 1977 Participants were so impressed with the evidence of the adverse effects of alcohol on pregnancy outcome that they requested NIAAA issue a public advisory about the risks posed by drinking during pregnancy. NIAAA's research staff was quite small at that time, and I found myself tasked with the responsibility for taking this on. Issuing such an advisory would be a daunting challenge since the prevailing view at the time, a vestige of post-prohibition backlash, was that any dose of alcohol was perfectly safe to consume during pregnancy. The advisory also would have to undergo a government review and approval process.

An agency of the U.S. federal government, NIAAA in 1977 was located within what was then called the Department of Health Education and Welfare (DHEW), which later became the Department of Health and Human Services, or DHHS. Issuing a public advisory would require the approval of DHEW. DHEW leaders were skeptical, and asked NIAAA for a "critical review" to justify the advisory. The task of preparing that review fell to me, but I was fortunate to have in hand a chapter on alcohol and pregnancy that Dr. Hank Rossett had written for the NIAAA Triennial Report to Congress that same year. With Dr. Rossett's chapter to provide an historical base, along with the reports from the February 1977 conference and many conversations with experts in the field, I compiled the "critical review," which rapidly received DHEW approval.

I then discovered that it also was my task to draft the advisory, while NIAAA leadership took the responsibility for finding appropriate venues for dissemination. It was decided to primarily target physicians and other health care professionals by publishing the advisory in two widely circulated government newsletters: The Food and Drug Administration (FDA) Drug Bulletin, and the Centers for Disease Control Morbidity and Mortality Weekly Report (CDC-MMWR). These publications were chosen because it was felt that unless the medical community was advised first there would be little, if any, impact on the public. Publication of the advisory, on June 1, 1977, was announced at a press briefing at DHEW Headquarters in Washington, D.C., an event which attracted major media attention.

Compared with subsequent advisories, recommendations made in the 1977 advisory were minimal. It warned against heavy drinking and advised women not to exceed two drinks per day if pregnant or trying to become pregnant. The rationale for this approach was based on the recognition that up until that time, drinking in pregnancy was considered to be safe. For the first time, we would be spreading the word to the medical and public communities that dangers appeared to be associated with heavy alcohol use in pregnancy. Thereby, we took the position of "safe in small amounts until proven dangerous" rather than our later position of "consider even small amounts to be a risk until proven safe".

The advisory attracted the attention of the U.S. Congress. The U.S. Senate called for hearings on whether alcoholic beverages should carry warning labels related to FAS. Two sets of hearings were held in the late 1970s. Congress decided not to impose beverage warning labels at that time. However, they did call for the preparation of a *Report to the President and Congress on Health Hazards Associated with Alcohol and Methods to Inform the General Public of these Hazards,* for which I was now tasked with preparing the background chapter on alcohol and birth defects. The joint conclusions prepared by the DHHS and the Department of the Treasury (which has responsibility for beverage alcohol labeling) made no recommendation for labeling. Rather, the Report called for the issuance of a U.S. Surgeon General's Advisory on Alcohol and Pregnancy. Once again I had the task of drafting an advisory, this time for the Surgeon General. This time though, the advisory took the conservative position of recommending that women not drink at all during pregnancy or if "at risk" for pregnancy. The Surgeon General's Advisory was issued in May, 1981 (FDA Drug Bulletin 1981). As we entered the 21st century, I was involved in drafting for then Surgeon General Carmona, an updated version of the Advisory which continued to recommend that women refrain from drinking in pregnancy.

In 1988 Congress once again considered the issue of alcoholic beverage labeling as a means to warn of the dangers of alcohol exposure in pregnancy and enacted the Alcoholic Beverage Labeling Act of 1988 (Public Law 100-690) which became effective in 1989. The U.S. thus became the first country to require warning labels related to pregnancy and drinking on alcoholic beverages. In 2005, the Surgeon General reissued an updated advisory on alcohol use and pregnancy that warned against FASD, the full spectrum of birth defects caused by prenatal alcohol exposure (U.S. Surgeon General, 2005).

Refs:

FDA Drug Bulletin. 1981. Surgeon general's advisory on alcohol and pregnancy. Jul;11(2):9-10.

Jones KL, Smith DW. 1973. Recognition of the fetal alcohol syndrome in early infancy. Lancet 302:999–1001.

Jones K, Smith D, Ulleland C, et al. 1973. Pattern of malformation in offspring of chronic alcoholic mothers. Lancet 301:1267–1271.

Lemoine P, Harousse H, Borteyru JP, et al. 1968. Children of alcoholic parents—anomalies in 127 cases. Arch Francaises De Pediatr 25: 830-832.

Ulleland C. 1970. Offspring of alcoholic mothers. Pediatr Res 4:474.

US Department of Transportation and US Department of Health and Human Services, 1980

US Surgeon General. 2005. Surgeon general's advisory on alcohol and pregnancy. Washington, DC: US Department of Health and Human Services.

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II. IMAGES: LOOKING AT FASD THROUGH THE EYES OF AN EMBRYOLOGIST

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About 30 years ago, images like those in Figure 1(page 27), were first published in a scientific journal [1]. Showing the remarkable similarity between the facial features recognized as being characteristic of full-blown Fetal Alcohol Syndrome (FAS) and those in a mouse fetus whose mother had been administered alcohol very early in her pregnancy, the images and the message that they convey continue to reinforce the value of basic FAS research.

The time in development when the mouse embryo had been exposed to alcohol corresponds to that in humans during the 3rd week after the egg is fertilized; when the embryo is in the form of a bi-layered disc of cells that is approximately 0.5 mm in diameter, and when most human pregnancies remain unrecognized.

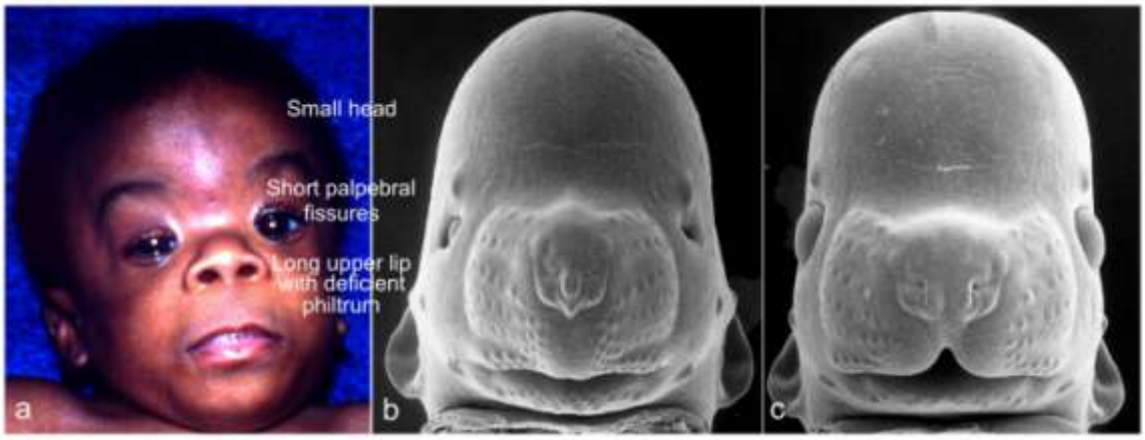

Figure 1. Illustrated are a child with Fetal Alcohol Syndrome (FAS; a), along with scanning electron micrographs of a prenatal alcohol-exposed (b) and a normal gestational day 14 fetal mouse (c). The abnormal facial features in the alcohol-exposed fetus are comparable to those that are characteristic of FAS. In the mouse, these defects result from maternal alcohol treatment at a time corresponding to the middle of the 3rd week of human development (modified from Sulik et al, 1981).

The fetal mouse images in Figure 1 were created using scanning electron microscopy (SEM). This methodology requires considerable finesse during the necessary tissue processing in order to prevent damage to the specimens and to allow acquisition of clean images. Briefly, the procedure entails dissecting the supporting tissues (chorionic and amniotic membranes) away from the embryos or fetuses, making free-hand cuts through the tissues at desired locations, dehydrating and critical point drying to remove all moisture, mounting the now ash-like specimens at the appropriate angle on adhesive-covered stubs, coating the specimens with vaporized heavy metal (typically a combination of gold and palladium), and then removing debris with a fine brush (typically made from a single eyelash) prior to viewing on the scanning electron microscope. The effort is worth it, with SEM providing a visual bonanza!

I first started imaging embryos with SEM as a postdoctoral fellow for the purpose of studying the genesis of birth defects. Examining the form of both abnormal and normal embryos at developmental stages that include those when the embryos are so tiny you can barely see them with the naked eye, to when all of the facial features are recognizable remains a bit like exploring the moon -- seeing many things in a way that few others, if any, have seen them before. For me, the creation of aesthetically appealing and informative embryo images has become kind of an art form; to some extent fulfilling my initial career interest in medical illustration. Indeed, it was a combined interest in art and biology that led to my pursuit of training in the anatomical sciences and subsequently to a research focus on birth defects.

The collection of embryo images acquired over the course of my academic career has been particularly useful for teaching. Typically, the 3D-like nature of the scanning electron micrographs (SEMs) makes the remarkable changes in form that occur during embryonic development much more readily understood than text, line drawings, or histological sections. A combination of these mouse and human SEMs have been prepared as an embryology tutorial entitled Embryo Images that is freely available on the internet (www.med.unc.edu/embryo-images). An additional series of SEMs of early human embryos that were prepared in my laboratory can be found at the following site: http://embryology.med.unsw.edu.au/wwwhuman/Stages/Stagesem.htm

During embryonic stages, the development and appearance of human and mouse embryos are quite similar. Shown in Figure 2 are human and mouse embryos of comparable developmental stages. In

both species, early development progresses as the small disc-like form of the day 7 mouse and the day 17 human elongates, and as the head and tail region become distinguishable as they curve toward each other. By day 11 in the mouse and by day 32 in the human the developing limbs can be recognized as small bulges on the sides of the body. Recognition of the developmental similarities in mouse and man, along with an understanding of the species differences, is essential to appreciating the value as well as the limitations of animal models of human disease.

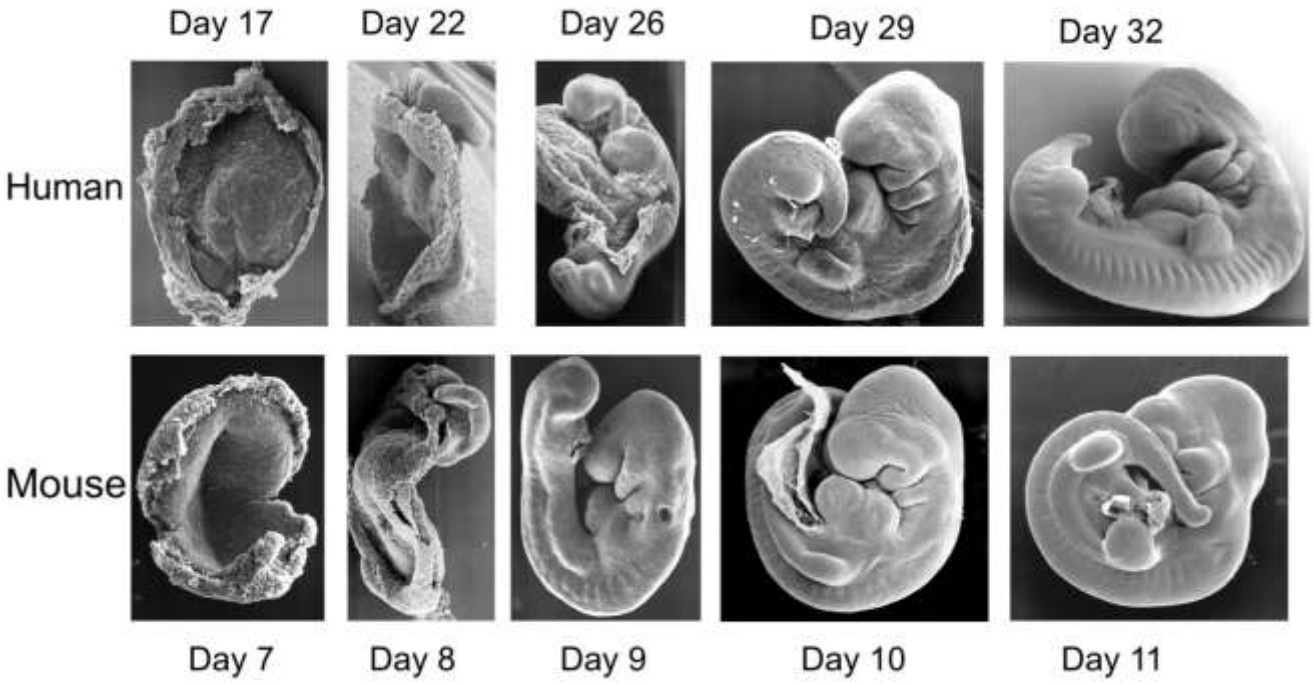

Figure 2. Scanning electron micrographs of comparably staged human and mouse embryos are shown.

Of course, a major difference in the development of mice and men is the duration of *in utero* life. A mouse's gestation period is approximately 20 days, while for the human it is usually 266 days (38 weeks). With mice normally being born prematurely as compared to people (i.e. at developmental stages that occur during the equivalent of the human 2nd trimester), a significant amount of FAS research employing the mouse as a model has entailed alcohol exposure during the first few days after their birth [2]. Work in my laboratory, however, has focused on the early stages of embryogenesis that occur from the beginning through the middle of the 2nd week of mouse development (days 7-11 of gestation; the stages shown in Figure 2). The corresponding developmental stages in humans are present from the middle of the 3rd week until the end of the 6th week after fertilization. For reference, Figure 3 provides a timeline of human embryonic development. The stage at which alcohol exposure causes an FAS-like face in mice (as shown in Figure 1) is that which is present in the middle of the 3rd week of human embryonic development. Alcohol exposure at later stages in mice also causes defects, some of which involve the facial region, but these defects are not those of "typical" FAS.

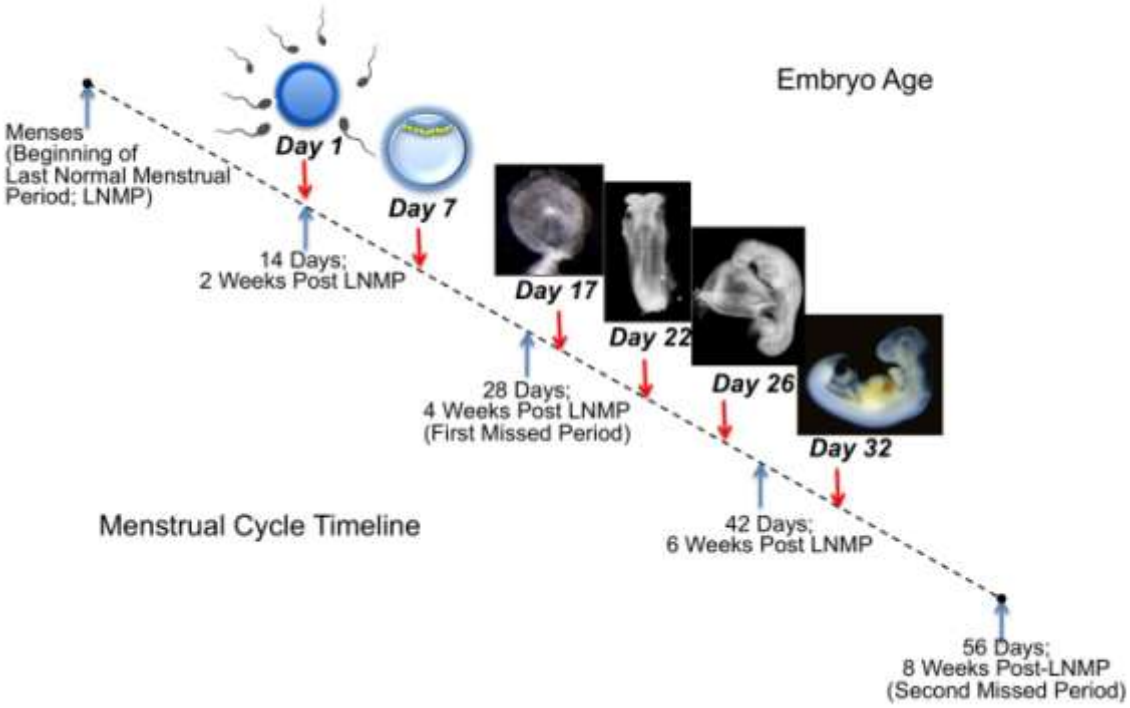

Figure 3. A timeline depicting early stages of human embryonic development illustrates embryonic age (above the dotted line) relative to time points during 2 normal menstrual cycles (below the dotted line). For this, a normal menstrual cycle is considered to be 28 days, with the timeline shown beginning at the initiation of the last normal menstrual period (LNMP). Although fertilization of the egg (day 1 of development) normally occurs 2 weeks following the LNMP, clinical pregnancy timelines routinely include the first 2 weeks of the cycle, adding them to the 38 week period of human gestation. Remarkable changes in form occur within the first few weeks, with a single cell rapidly dividing to generate an embryo that by the end of the first week is comprised of 2 distinct cell layers. By early in the third week (day 17) the head and tail ends of the bilayered disc of cells can be distinguished and the brain begins to form. From day 22 to 32 the embryo elongates as the head and tail end curve toward each other. Please note that embryo sizes are not shown to scale.

While the face of full-blown FAS has proven diagnostically significant, understanding that the facial changes reflect those involving the brain is critical to fully appreciating prenatal alcohol-mediated damage. A substantial amount of work in my laboratory has employed SEM and routine histological methods to show alcohol-induced reductions in the midface and also in the forebrain of mice following gestational day 7 or 8 alcohol exposure [3-6]. These defects present as a range of phenotypes having varying degrees of severity. Recently, the availability and application of new imaging methodologies have facilitated further analyses of the insult to fetal and postnatal mice that follows a number of different acute alcohol exposure times during embryogenesis [7-9]. The methodologies being employed are high-resolution magnetic resonance imaging (a.k.a. magnetic resonance microscopy, MRM) along with diffusion tensor imaging (DTI), the latter of which allows detailed analyses of brain fiber tracts. Similar to magnetic resonance-based human brain images (MRIs), the mouse MRM brain scans can be viewed individually or can be compiled as 3D reconstructions. The clarity of the individual high-resolution scans allows distinction between a number of brain regions; regions that can then be compared in alcohol-exposed and unexposed animals. The images in Figure 4 a-d are exemplary of this. Shown are 3D reconstructions of the brain of one normal (a) and three abnormal gestational day 17 fetuses (b-d) that were affected to varying degrees by maternal exposure to alcohol limited to the 7th day of gestation. In the affected brains, the major changes involve the cerebrum and olfactory bulbs. For the cerebrum, the tissues located close to the midline are deficient, resulting in

abnormally close approximation of the olfactory bulbs. The affects can be asymmetric, and can include volume reductions to complete absence of the olfactory bulbs.

Just as the brain images can be reconstructed from individual MRM scans, so can the structures surrounding the brain. The images in Figure 4 e-h were prepared by reconstructing the facial surfaces of the animals whose brains are shown. In the alcohol-exposed fetuses, varying degrees of abnormally close proximity of the nostrils accompanied by median upper lip alterations are readily seen. As for the brain, this reflects a midline tissue deficiency. In the animals shown in this figure, a direct correlation between the degree of facial and brain involvement is evident.

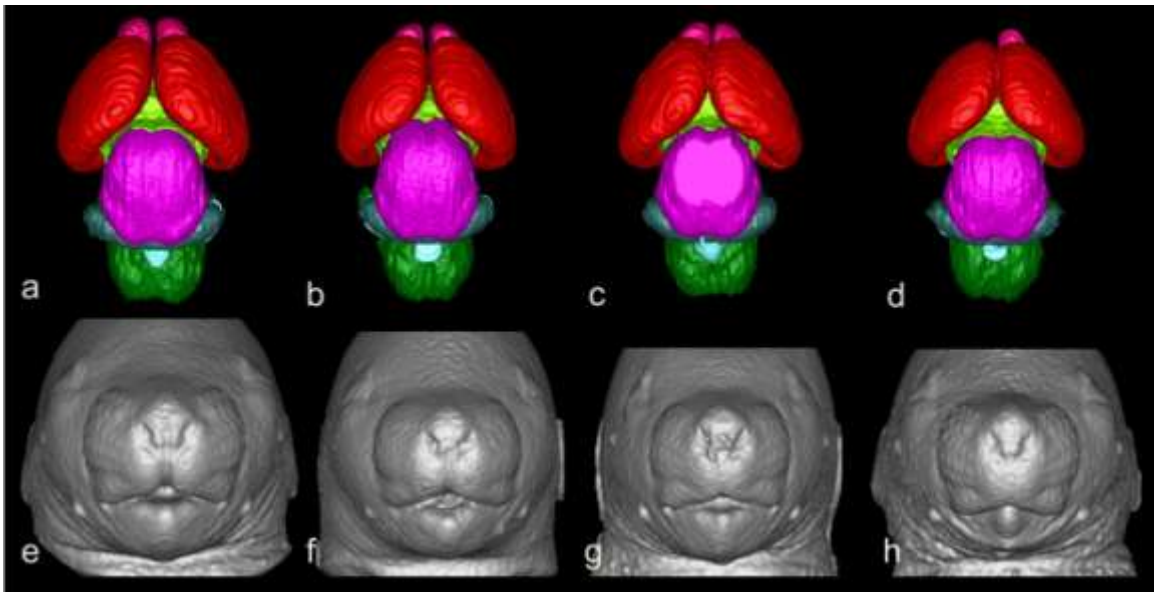

Figure 4. Shown are reconstructed magnetic resonance microscopy (MRM) images of the brain and face of a normal gestational day 17 fetal mouse (a, e), along with those from 3 fetuses that had been exposed to alcohol on their 7th gestational day (b, f; c, g; d, h). As compared to the normal fetus, the affected fetuses have varying degrees of olfactory bulb [bright pink structures at the top (front) of the brain] deficiency. Also notable in (c) is the abnormally close proximity of the two olfactory bulbs and of the cerebral hemispheres (red structures). The latter are not separated by a deep interhemispheric groove as in the normal brain. The faces of the alcohol-exposed mouse fetuses (f-h) show a characteristically small nose, with the nostrils being too closely approximated, accompanied by a long (from nose to mouth) central portion of the upper lip that is lacking its normal central groove. The animal in (h) also has an obviously small lower jaw (mandible). Brain region color codes are as follows: Pink = olfactory bulbs; Red = cerebral hemispheres; Light green = diencephalon; Magenta = mesencephalon; Teal = cerebellum; Dark green = hindbrain (minus cerebellum).

Importantly, recent magnetic resonance-based examination of postnatal mice following gestational day 7 alcohol treatment has illustrated that the morphological damage caused by this isolated early exposure is permanent. Most notable has been the finding that the corpus callosum (CC), the major fiber tract that connects the two cerebral hemispheres is deficient [10]. As shown in Figure 5, in two variably affected alcohol-exposed postnatal day 45 mice, the CC appears similar to that in individuals with FAS.

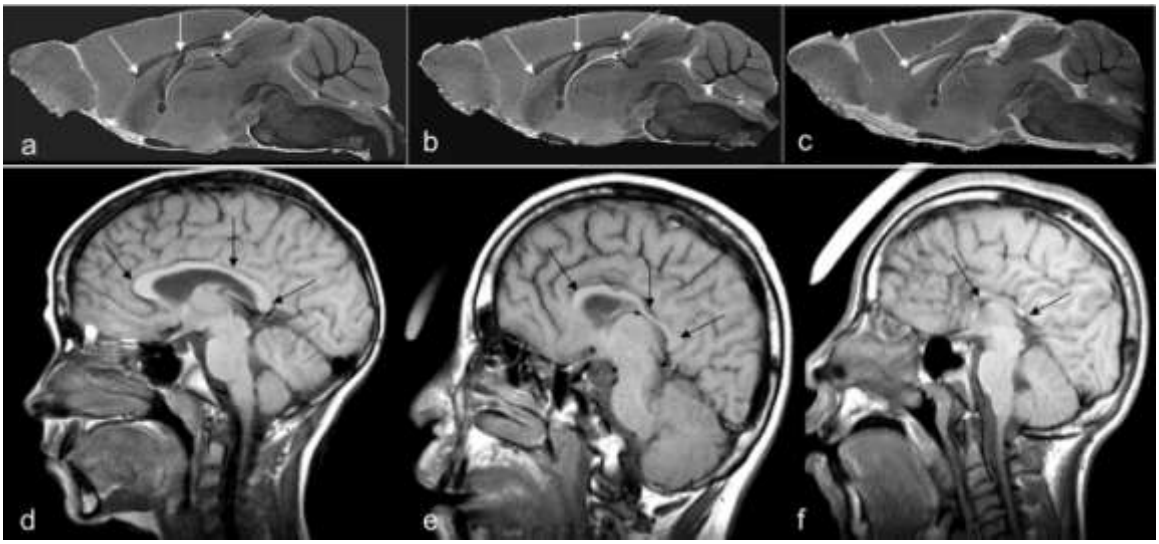

Figure 5. Magnetic resonance imaging (MRI) of prenatal alcohol-exposed 45 day old mice and individuals with fetal alcohol syndrome (FAS) illustrate comparable corpus callosum (CC) dysmorphology as shown in midsagittal scans. The normal form of the mouse CC is shown in a (dark structure indicated by arrows), and in a child (light structure indicated by arrows in d). Subsequent to prenatal alcohol exposure on gestational day 7, moderate thinning, which is particularly notable in the mid-region of the CC is apparent in the mouse brain shown in the MRI in b. In an MRI from a more severely affected animal shown in c, the middle of the CC appears to be completely absent. In this animal, the anterior and posterior aspects of the CC, although reduced in size, remain evident (arrows). These defects appear remarkably similar to those in two variably affected FAS patients (e and f; human MRIs are courtesy of Dr. S. Mattson).

While this work has convincingly shown that alcohol can cause permanent damage to the brain when exposure occurs at very early developmental stages, it is also clear that the developing brain remains vulnerable at later stages to alcohol-mediated defects [11-14]. Of course, a major problem associated with the very early exposure times, is that most women remain unaware of their pregnancy. This strongly supports the need for a universal approach to prevention-directed educational efforts and to pre-pregnancy counseling. With the belief that such age-appropriate educational efforts should be provided for students that are in their pre-and early teens, we have developed a middle school curriculum entitled "Better Safe Than Sorry: Preventing a Tragedy". A unique feature of this curriculum is that it employs a hands-on science approach that allows the students to see for themselves the deleterious effects of alcohol exposure during development. The organisms that are used for an experiment that the students conduct as part of the curriculum are brine shrimp (Artemia), small aquatic Crustacians. This curriculum is freely available at the following website: http://pubs.niaaa.nih.gov/publications/Science/curriculum.html. Currently, another curriculum that is directed toward high school-age students and that features a virtual experiment and a video designed for use in health and parenting classes is being finalized. Both curricula emphasize the fact that alcohol can cause permanent damage to an unborn baby even prior to the time that pregnancy is typically recognized.

Included in the previous Forum E-letter (Issue 3, May, 2010) was the full text of a recent paper from my laboratory [8]. The world-wide exposure that this has provided for our basic research results, along with the opportunity to further describe herein our laboratory's work and findings are highly valued. It is my hope that this information, along with the images that we have created, will also be employed by others to advance FASD education and prevention efforts.

Acknowledgements
Much of the work described was conducted by graduate and postdoctoral fellows in the Sulik laboratory. Most recently, these include Drs. Elizabeth Godin, Robert Lipinski, Shonagh O'Leary-Moore, and Scott Parnell. In addition, the excellent technical support of Deborah Dehart and assistance with 3D facial imaging by Dr. Peter Hammond have been invaluable. The described curricula have been developed with Drs Marianne Meeker and Gary Duncan. This work was funded by NIH/NIAAA grants RC1 AA019211, T32 AA007573, P60 AA11605, U01 AA017124, and R44 AA018245; National Center for Research Resources/National Cancer Institute grants P41 05959 and U24 CA092656; and the University of North Carolina Neurodevelopmental Disorders Research Center grant HD 03110. Some of these investigations were conducted in conjunction with the Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD). Additional information about CIFASD can be found at www.cifasd.org

References

[1] K.K. Sulik, M.C. Johnston, M.A. Webb, Fetal alcohol syndrome: embryogenesis in a mouse model, Science 214 (1981) 936-938.

[2] J.W. Olney, D.F. Wozniak, N.B. Farber, V. Jevtovic-Todorovic, P. Bittigau, C. Ikonomidou, The enigma of fetal alcohol neurotoxicity, Ann Med 34 (2002) 109-119.

[3] K.K. Sulik, M.C. Johnston, Embryonic origin of holoprosencephaly: interrelationship of the developing brain and face, Scan Electron Microsc (1982) 309-322.

[4] L.E. Kotch, K.K. Sulik, Experimental fetal alcohol syndrome: proposed pathogenic basis for a variety of associated facial and brain anomalies, Am J Med Genet 44 (1992) 168-176.

[5] U.B. Schambra, J.M. Lauder, P. Petrusz, K.K. Sulik, Development of neurotransmitter systems in the mouse embryo following acute ethanol exposure: a histological and immunocytochemical study, Int J Dev Neurosci 8 (1990) 507-522.

[6] K.K. Sulik, M.C. Johnston, Sequence of developmental alterations following acute ethanol exposure in mice: craniofacial features of the fetal alcohol syndrome, Am J Anat 166 (1983) 257-269.

[7] S.E. Parnell, S.K. O'Leary-Moore, E.A. Godin, D.B. Dehart, B.W. Johnson, G. Allan Johnson, M.A. Styner, K.K. Sulik, Magnetic resonance microscopy defines ethanol-induced brain abnormalities in prenatal mice: effects of acute insult on gestational day 8, Alcohol Clin Exp Res 33 (2009) 1001-1011.

[8] E.A. Godin, S.K. O'Leary-Moore, A.A. Khan, S.E. Parnell, J.J. Ament, D.B. Dehart, B.W. Johnson, G. Allan Johnson, M.A. Styner, K.K. Sulik, Magnetic resonance microscopy defines ethanol-induced brain abnormalities in prenatal mice: effects of acute insult on gestational day 7, Alcohol Clin Exp Res 34 (2010) 98-111.

[9] S.K. O'Leary-Moore, S.E. Parnell, E.A. Godin, D.B. Dehart, J.J. Ament, A.A. Khan, G.A. Johnson, M.A. Styner, K.K. Sulik, Magnetic resonance microscopy-based analyses of the brains of normal and ethanol-exposed fetal mice, Birth Defects Res A Clin Mol Teratol.

[10] S.K. O'Leary-Moore, S.E. Parnell, E.A. Godin, K.K. Sulik, Magnetic resonance-based studies of fetal alcohol spectrum disorder in animal models, Alcohol Research and Health (In press).

[11] J.R. West, W.J. Chen, N.J. Pantazis, Fetal alcohol syndrome: the vulnerability of the developing brain and possible mechanisms of damage, Metab Brain Dis 9 (1994) 291-322.

[12] J.W. Olney, Fetal alcohol syndrome at the cellular level, Addict Biol 9 (2004) 137-149; discussion 151.

[13] M.W. Miller, Brain development : normal processes and the effects of alcohol and nicotine / edited by Michael W. Miller, Oxford University Press, Oxford ; New York, 2006.

[14] C.R. Goodlett, K.H. Horn, F.C. Zhou, Alcohol teratogenesis: mechanisms of damage and strategies for intervention, Exp Biol Med (Maywood) 230 (2005) 394-406.

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III. SOME INSIGHTS ABOUT THE USE OF ETHANOL DURING PRENATAL AND EARLY POSTNATAL PERIODS IN ARGENTINA

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Currently in Argentina as well as in the majority of countries of South America, there is not epidemiological information available about the prevalence rate of FASD similar to those established for other countries (such as the United States of America and European countries). There has been no research that has assessed women's alcohol consumption patterns during pregnancy and lactation. Nor do we know about the prevalence of alcoholism, alcohol abuse, and fetal alcohol syndrome among Argentines, or the quantity and frequency of drinking among the general population of the country. Although this specific information is lacking, the magnitude of the problem is indicated by finding that liver cirrhosis was ranked as one of the principal causes of deaths in Argentina during the 1980s [1]. Moreover, a report by the Pan American Health Organization indicated that alcoholism remains one of the top pathologies in Argentina, with its greatest impact being among the country's youth [2].

There are few scientific groups authorized to analyze ethanol effects during pregnancy and/or lactation, in this region of the world. From 1986 until now, the laboratory at the *Instituto de Investigaciones Médicas Mercedes y Martín Ferreyra* (the Mercedes and Martín Ferreyra Institute of Medical Research), in Córdoba, Argentina, has shown that alcohol consumption amongst rats during pregnancy and lactation leads to the infant rats having alcohol-related sensory memories that increase their alcohol consumption later in life [3 -5]. Some of these findings have recently been extended to human infants born at the *Hospital Universitario de Maternidad y Neonatología* (University Maternity and Neonatology Hospital), also in Córdoba. Newborns of women who drank moderately during pregnancy, exhibited heightened reactivity to the smell of alcohol in comparison to newborns of women who drank less [6]. Because maternal ethanol consumption distinctly flavours mother's milk [7,8], and such changes are detected by the infant [7,8,9], a large body of research has shown that sensory learning also occurs when the infant experiences alcohol in its mother's milk [9, 10].

In explorative research conducted by Iveli et al. (2007), a random sample of pregnant women who gave birth within the Maternity Service of the Hospital Interzonal General de Agudos "General San Martín" of La Plata, Argentina, shows the effects of light maternal ethanol consumption during pregnancy on the appearance of minor malformations in neonates [11]. One of the main findings regarding newborns of light drinking mothers was that the 66% of them presented at least one type of

minor anomaly/malformation, particularly retromicrognathia and ear/preauricular anomalies. This is in accordance with the fact that cranial and facial malformations are the most common features of FASDs [12]. It must be taken into account that in addition to inducing facial dysmorphism, ethanol can affect the development of neural structures, particularly the brain [13] and ocular system [14]. A study conducted in two important medical centres of Montevideo, Uruguay (Hospital Pereira Rossell - the first maternity centre of the country - and the Hospital de Clínicas - Hospital dependent of the National University), estimated the prevalence of drug consumption during pregnancy by interviewing women and analyzing biological samples to investigate the risk of drug consumption at this time [15]. Through the survey, the results about consumption during pregnancy were: 41.3 % for tobacco, alcohol 36.8%, tranquilizers 16.3% and cannabis 1.5%. The analysis of babies' meconium samples showed 51.8% for tobacco, 43.5% for alcohol, 2.5% for tranquilizers and 2% for cannabis. 11 % of all newborns had low birth weight and 14.8 % had health problems [15].

Beliefs about the medicinal properties of alcohol attain particular importance during pregnancy and lactation. The tradition of many cultures suggests that alcohol consumption and usage can benefit both mothers and infants. Medical practice dating back to the 1800s indicates that soaking the umbilical cord with alcohol prevents umbilical infections and accelerates cord detachment [16]. Although this practice is limited to cleaning the cord stump in some countries [16-18], the practice of treating the cord stump with gauze soaked with 180-proof ethyl alcohol persists in some Latin America countries [19]. It is important to emphasize here that this practice can lead to significantly high blood alcohol concentrations in the infant [19, 20].

Another long-standing belief is that drinking alcohol has galactogenic (milk producing) results for lactating women [21]. These women are often advised that consuming alcohol will improve the quality and quantity of their milk, facilitate milk letdown, and help their babies get a good night's sleep [22]. The type of beverage believed to possess galactogenic properties varies among cultures. For example, women in Mexico are encouraged to drink as much as two litres daily of pulque (a low-alcohol beverage made of a local fruit, *Agave atrovirens*) during both pregnancy and lactation [23]. Indochinese women in California drink wine steeped with herbs [24]. The belief that alcoholic beverages are galactagogues is ingrained in current-day medical practice in the United States. That is evident from a recent study conducted in my country [25], which found that the majority of lactating women reported that health professionals advised them to abstain from drinking during pregnancy. However, one-quarter of the women reported that they were encouraged to consume alcohol once they began lactating.

In Argentina, as in other cultures, beliefs exist about the medicinal properties of alcohol during the peripartum and lactational periods. This study [25] indicated that, the large majority (93.4%) of the mothers surveyed at local medical clinics, in city plazas, and outside shopping malls in Buenos Aires and Córdoba (Argentina), reported that they had used alcohol to clean the umbilical cord stump. Moreover, 26.9% of the mothers who used alcohol to treat the cord stump still practiced the age-old tradition of soaking the cord stump with bandages containing ethyl alcohol, with the belief that such practices protected the cord from infection and facilitated its detachment. Although smaller in number, some of the women also reported that they applied warm cloths soaked in alcohol to the infant's stomach area to alleviate a stomachache. In addition to this, approximately half of the women reported that they had received medical advice about drinking alcoholic beverages during pregnancy. However, only a quarter of the women received such advice during lactation. This low rate of health professionals advising women about alcohol consumption during lactation was not due to a lack of interaction between the physician and the woman, since each woman in the study reported visiting the doctor at least once during the pregnancy and once during the postpartum period. Clinical research has shown that women who received advice from a physician to abstain from alcohol reported a lower risk of drinking during pregnancy [26].

Therefore, there is a need to develop culturally appropriate professional development strategies to

increase both health professionals' and patients' awareness of the risks of alcohol consumption during pregnancy and lactation, and to provide accurate information to both of those groups on the risks of alcohol exposure to the fetus and neonate. Research now taking place in Argentina [3-5], Spain [27] and in the United States [7,21,28,29] aims to determine how beliefs about alcohol's efficacy and its hazards affect the behaviour of the mother and, in turn, an infant's responsiveness to alcoholic beverages as a result of early sensory experiences.

References

1.Hauger-Klevene JH, Balossi EC. Liver cirrhosis mortality in Argentina: its relationship to alcohol intake. Drug Alcohol Depend 1987;19 (1):29–33.

2.Pan American Health Organization. Profile of the health services system Argentina. 2nd ed. Available from:http://www.lachsr.org/documents/healthsystemprofileofargentina-EN.pdf.

3. Abate P, Pueta M, Spear NE, Molina JC. Fetal learning about ethanol and later ethanol responsiveness: evidence against "safe" amounts of prenatal exposure. Exp Biol Med 2008;233:139-54.

4. Pepino MY, Abate P, Spear NE, Molina JC. Heightened ethanol intake in infant and adolescent rats after nursing experiences with an ethanol-intoxicated dam. Alcohol ClinExp Res 2004;28(6):895–905.

5. Spear NE, Molina JC. Fetal or infantile exposure to alcohol promotes ethanol ingestion in adolescence and adulthood: a theoretical review. Alcohol Clin Exp Res 2005;25:909-29.

6. Faas AE, Sponton ED, Moya PR, Molina JC. Differential responsiveness to alcohol odor in human neonates: effects of maternal consumption during gestation. Alcohol 2000;22(1):7–17.

7. Mennella JA, Beauchamp GK. The transfer of alcohol to human milk. Effects on flavor and the infant's behavior. N Engl J Med 1991;325 (14):981–5.

8. Mennella JA, Beauchamp GK. Effects of beer on breast-fed infants. JAMA 1993;269(13):1637–8.

9. Mennella JA. Infants' suckling responses to the flavor of alcohol in mothers' milk. Alcohol Clin Exp Res 1997;21(4):581–5.

10. Mennella JA, Beauchamp GK. Infants' exploration of scented toys: effects of prior experiences. Chem Senses 1998;23(1):11–7.

11. Iveli MF, Morales S, Rebolledo A, Savietto V, Salemme S, Apezteguía M, Cecotti N, Drut R, Milesi V. Effects of light ethanol consumption during pregnancy: increased frequency of minor anomalies in the newborn and altered contractility of umbilical cord artery. Pediatr Res. 2007 Apr;61(4):456-61.

12. Eustace LW, Kang DH, Coombs D 2003 Fetal alcohol syndrome: a growing concern for health care professionals. J Obstet Gynecol Neonatal Nurs 32:215–221.

13. Dunty WC Jr, Zucker RM, Sulik KK 2002 Hindbrain and cranial nerve dysmorphogenesis result from acute maternal ethanol administration. Dev Neurosci24:328–342

14. Parnell SE, Dehart DB, Wills TA, Chen SY, Hodge CW, Besheer J, Waage-Baudet HG, Charness ME, Sulik KK 2006 Maternal oral intake mouse model for fetal alcohol spectrum disorders: ocular defects as a measure of effect. Alcohol Clin Exp Res 30:1791–1798

15. Magri R, Míguez H, Parodi V, Hutson J, Suárez H, Menéndez A, Koren G, Bustos R 2007

Consumo de alcohol y otras drogas en embarazadas. Arch Pediatr Urug 2007; 78(2):122-132.

16. Dore S, Buchan D, Coulas S, Hamber L, Stewart M, Cowan D, et al. Alcohol versus natural drying for newborn cord care. J Obstet Gynecol Neonatal Nurs 1998;27(6):621–7.

17. Golombek SG, Brill PE, Salice AL. Randomized trial of alcohol versus triple dye for umbilical cord care. Clin Pediatr (Phila) 2002;41 (6):419–23.

18. Janssen PA, Selwood BL, Dobson SR, Peacock D, Thiessen PN. To dye or not to dye: a randomized, clinical trial of a triple dye/alcohol regime versus dry cord care. Pediatrics 2003;111(1):15–20.

19. Choonara I. Percutaneous drug absorption and administration. Arch Dis Child 1994;71:F73–F74.

20. Dalt LD, Dall'Amico R, Laverda AM, Chemollo C, Chiandetti L. Percutaneous ethyl alcohol intoxication in a one-month-old infant. Pediatr Emerg Care 1991;7(6):343–44.

21. Mennella, JA. The transfer of alcohol to human milk: sensory implications and effects on motherinfant interaction. In: Hannigan, JH.; Spear, N.; Spear, L.; Goodlett, CR., editors. Alcohol and alcoholism: brain and development. Hillsdale: Lawrence Erlbaum Associates;1999. p. 177-98.

22. Mennella, JA. Alcohol use during lactation: the folklore versus the science. In: Auerbach, KG., editor. Current issues in clinical lactation. Boston: Jones and Bartlett Publishers; 2002. p. 3-10.

23. Flores-Huerta S, Hernández-Montes H, Argote RM, Villalpando S. Effects of ethanol consumption during pregnancy and lactation on the outcome and postnatal growth of the offspring. Ann Nutr Metab 1992;36(3):121–8.

24. Fishman C, Evans R, Jenks E. Warm bodies, cool milk: conflicts in post partum food choice for Indochinese women in California. Soc Sci Med 1988;26(11):1125–32.

25. Pepino MY, Mennella JA. Advice given to women in Argentina about breast-feeding and the use of alcohol. Rev Panam Salud Publica. 2004Dec;16(6):408-14.

26. Jones-Webb R, McKiver M, Pirie P, Miner K. Relationships between physician advice and tobacco and alcohol use during pregnancy. Am J Prev Med 1999;16(3):244–7.

27. Chotro MG, Arias C, Laviola G. Increased ethanol intake after prenatal ethanol exposure: studies with animals. Neurosci Biobehav Rev. 2007;31(2):181-91.

28.Mennella, JA. Watson, R. Nutrition and alcohol. Second edition. Boca Raton: CRC Press; 2004. Alcohol use during lactation: effects on the mother and breastfeeding infant; p. 377-91.

29. Petrov ES, Varlinskaya EI, Spear NE. Reinforcement from pharmacological effects of ethanol in newborn rats. Alcohol Clin Exp Res 2003;27(10):1583–91.

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IV. THE PATH TO JUSTICE FOR INDIVIDUALS WITH FASD

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Air Canada's flight AC8447 from Vancouver, B.C. winged its way to Canada's Yukon on September 8, 2008. David Boulding and I watched the Fall scenery unfold; the mountains, accessorized with boas of sunshiny yellow Aspen trees wherever a stream cut its way down the mountainside, were a gorgeous sight. We dipped into a valley, flew over the Yukon River and landed at the Whitehorse airport. David, an attorney from B.C. is a man with a crusade. His awareness of both the prevalence of FASD in the justice system and the lack of recognition of it among court professionals drives him to travel the world over, wherever he can find English-speaking judges, attorneys, police officers, corrections officers and others with whom he can talk.

Both David and I had mused over the fact that this meeting to come, with the Canadian government bringing together North Americans interested in FASD from many aspects of the juvenile and criminal justice system, was the first such meeting of its kind anywhere in the world. Long overdue, we both thought, but, simultaneously, shook our heads in amazement that this meeting had been conceived and organized, not in Ottawa, but in a very small and remote community in the Yukon, best known for the Klondike Gold Rush, and where the extreme Winter cold necessitates electrical plugs on the street to keep parked cars warm enough to start.

Little did we know that this conference might lead in two years to a resolution of the Canadian Bar Association on FASD as an access to justice issue and agreement from Canadian Justice Ministers that they share "strong support" to make FASD and the justice system a "priority".

The conference Steering Committee, formed in 2007, included fourteen participants from the justice system, eleven of whom were Yukon-based. This group of individuals had realized the nature and extent of the problem and were determined to raise North American, if not worldwide, consciousness of how those disabled by brain damage from prenatal alcohol exposure were denied justice should they find themselves in trouble with the law. The Steering Committee included representatives from government, from the judicial system, from law enforcement, from the Canadian Bar Association, from the Native community, from Canadian Justice research and from a local grassroots organization, Fetal Alcohol Spectrum Society Yukon (FASSY).

The approximately 112 delegates included judges, Royal Canadian Mounted Police representatives, prosecutors, probation officers, defense attorneys, academics, law professors, Aboriginal advisors, FASD diagnosticians, police officers and others.
The two days of meetings included an overview of the disability by Dr. Sterling Clarren, a medical doctor from the University of Washington, in Seattle, an FASD researcher and CEO of the Canadian NW FASD Research Network and a keynote talk by Judge Mary Ellen Turpel-Lafond. Judge Turpel-Lafond, as quoted in the excellent summary of the conference prepared by Charlotte Fraser, explained that underlying improving access to justice for individuals with FASD "…is the desire in fact to understand and keep them out of the justice system and to ensure that the justice system is not used as a substitute for appropriate social services and supports for some of our most vulnerable citizens."

It was pointed out that those with FASD are more at risk of coming into contact with the justice system because of their cognitive impairments and that once in the system they may have difficulty applying for legal representation, may have impaired ability to participate in meetings and attend court, may

have difficulty understanding what is taking place, may be unable to understand or act on their attorney's advice, may falsely confess to acts they didn't commit and may be unable to comply with the conditions of their release. Professor Ken Roach from the Faculty of Law at the University of Toronto reviewed Canadian case law and found that few with FASD have not been held criminally responsible for their actions. He points out "The justice system is premised on assumptions that people act in a voluntary manner that is determined by free will and that they can make informed and voluntary choices both with respect to the exercise of their rights and the decision to commit crimes. Contrary to the reality of the permanent brain damage caused by FASD, it is also assumed that mental disorders can be treated so that a person will eventually either be found fit to stand trial or to present no substantial danger to the public and therefore be safe to release."

In attempting to answer why the justice system is not better at responding to FASD, the question of access to diagnostic services arose. If those in the system, after participating in FASD training, recognize that FASD might be present, to whom do they turn for confirmation of their suspicions? Can a Canadian court order an FASD assessment? Who will bear the financial responsibility of the ordered assessment. In Canada the courts may order an assessment as long as there are client resources for funding. If, however, there are no private resources to pay for an assessment, an application for funding must be made with an organization such as the FASD Youth Justice Project in Winnipeg. These local projects and groups are not found in every Canadian community, however. In the U.S., the courts, generally, have resources to pay for retaining experts to assist in the defense of indigent clients. Payment for an FASD assessment would fall into this category. In Canada, adult FASD diagnostic reports can be ordered to assess fitness to stand trial and issues of criminal responsibility but cannot be ordered to assist the court in determining an effective and appropriate sentence.

Recommendations to improve access to justice for those with FASD included 1) education and awareness: FASD training for justice professionals, 2) identification: find ways to screen for and diagnose FASD within the justice system, 3) information sharing and establishing linkages: encourage collaboration and information sharing between various government departments such as education, housing, social services and health and, 4) specialized programming and initiatives: develop wrap-around services and special support persons and systems to assist those with FASD who are in the justice system. The overarching goal should be community-based programming rather than incarceration.

During the conference we were told about another first in Canada and elsewhere; the Yukon Community Wellness Court in Whitehorse. A recent addition to the treatment courts in Whitehorse, Wellness Court meets twice monthly. It is a judicially supervised therapeutic court providing treatment and support for offenders living with an addiction to alcohol or other drugs, a mental health problem, or an intellectual disability including but not limited to FASD. The court is involved in on-going work to develop more effective measures to monitor offender behavior and to reduce recidivism by providing more comprehensive supports. Participants in the Wellness Court collaborate with the judge and court staff to develop an individualized plan and are provided whatever is necessary for them to achieve goals all can agree on. If the offender succeeds in maintaining his/her sobriety and commits no new offenses during the 12-18 months of the program, the result is the imposition of a community-based sentence and, in some instances, the closing of the case. Once accepted to the Wellness Court, defenders are offered referrals for detoxification, substance abuse counseling, mental health assessment and treatment as well as a medical assessment and treatment. Participants are also required to provide breath and/or urine samples to confirm they are in compliance with court orders to refrain from the use of alcohol or other drugs. The court has a range of incentives to re-enforce compliance and a range of sanctions for non-compliance. The therapeutic court works by using the respected authority of the court combined with the personalized interest of the judge and the court staff to support the offender in meeting his/her program goals.

David and I were invited to have lunch with the staff and clients at the offices of the Fetal Alcohol Spectrum Society Whitehorse (FASSY). At the time FASSY was preparing a hot lunch daily for their approximately thirty adult clients, all diagnosed with FASD. FASSY was, in 2008, funded by Public Safety and Emergency Preparedness Canada in order to test this model of service delivery. Funding enabled FASSY to pay for FASD diagnostic assessments. Some housing was provided through apartments over the FASSY offices. The tasty lunch, prepared both on site and in the home kitchens of the staff, clearly provided the clients the anchor of a big, animated functional family with lots of caring parents and many siblings. This was, according to the clients, the only actual meal many would have all day. Day trips and outings were planned regularly for the clients. Such a model could be developed widely with government support.

Following the Conference, a number of activities were developed to address some of the barriers faced by individuals with FASD coming in contact with the justice system. However, one of the potentially most significant was the Resolution of the Canadian Bar Association (CBA) which was prepared by lawyers who are members of the Yukon Branch of the CBA. One of the lawyers was Rod Snow, a member of the Conference Steering Committee, past President of the CBA Yukon, and now, the President of the CBA. The CBA is the voice of the legal profession in Canada with over 37,000 members.

Rod Snow and the CBA Yukon had quietly supported the idea of the Conference from the very beginning. After attending the Conference, he determined that the issue of FASD in the justice system needed to be brought to a national stage. As incoming President of the Canadian Bar Association he encouraged his friends in the CBA Yukon to sponsor the Resolution.

Mr. Snow observes, “As to FASD, there is a strong desire across the (Canadian) North to do things differently.” This Resolution, passed by the governing CBA Council at the CBA annual meeting in mid-August 2010, now represents CBA national policy and has captured a great deal of media attention and some editorial support. Mr. Snow was quoted in the Montreal Gazette on August 16, 2010 noting “Judges see people before them repeatedly who are probably there in large measure because of a permanent organic brain injury.”

Following the passage of the Resolution, the Times Colonist, Victoria, B.C. wrote, August 18, 2010, “It is both unfair and unwise to keep imprisoning people with fetal alcohol syndrome.” They note “Prison sentences are intended, among other purposes, to deter and rehabilitate offenders. The threat of jail is supposed to make people think twice before committing a crime. That doesn’t work with many people suffering from fetal alcohol syndrome.” The article quotes the estimate by Dr. Christine Loock, an FASD researcher from the University of British Columbia, that one in four inmates is imprisoned because of offenses linked to FASD. The Times Colonist supports the CBA’s Resolution on FASD and access to justice and applaud a new approach, calling it “…common-sense...” and a saving to taxpayers. They conclude “The time for talking is long past. We know what we are doing is costly, ineffectual and cruel. Action is overdue.”

Federal Justice Minister and Attorney-General for Canada, Rob Nicholson attended the CBA meeting two days after the Resolution was passed. In response to a question from a Yukon lawyer he said that FASD was a “huge problem in our system” and committed to keep the issue on the Canadian Justice Ministers agenda.

The Resolution first describes the range of problems experienced by those with FASD, notes sentencing options now available are often ineffective in changing behavior, points out those with FASD are entitled to equality under the law without discrimination, recognizes the Federal, Provincial and Territorial Ministers responsible for justice have established an initiative as to access to justice for those with FASD and then offers the following three CBA Resolutions:

1. Support the initiative of Federal, Provincial and Territorial Ministers responsible for justice with respect to access to justice for people with FASD and urge all levels of government to allocate additional resources for alternatives to the current practice of criminalizing individuals with FASD

2. Urge the federal, territorial and provincial governments to develop policies designed to assist and enhance the lives of those with FASD and to prevent persistent over-representation of FASD affected individuals in the criminal justice system

3. Urge the federal government to amend criminal sentencing laws to accommodate the disability of those with FASD

At their October 14-15, 2010 annual meeting, the Canadian Federal-Provincial-Territorial Ministers responsible for Justice agreed to a joint communique stating that among the key justice and public safety issues to which they were committed was Fetal Alcohol Spectrum Disorder (FASD) and Access to Justice. They noted that "Fetal Alcohol Spectrum Disorder (FASD) affects many offenders and victims who deal with the justice system. There was strong support to continue to make FASD and the justice system a priority item and to engage the CBA in dialogue about FASD as an access to justice issue."

I could not have imagined at the Whitehorse Conference, a scant two years ago, that the Canadian government would be engaged with this issue at this level. The Conference Steering Committee and, in particular, Rod Snow, utilized the conclusions of the Conference and brought this issue to the consciousness of an entire country. What an amazing outcome. And, of course, this can and should be a model for other countries such as the U.S. and the American Bar Association. To say I feel honored to have been witness to this historic development doesn't fully capture the depth of my gratitude to all who were instrumental in the passage of Resolution 10-02-A. This Resolution and the Ministers' response will give David Boulding plenty to talk about wherever in the wide world he goes.

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PubMed, Synapse. 2010 Oct 20. [Epub ahead of print]

1) VITAMIN C PROTECTS AGAINST ETHANOL AND PTZ-INDUCED APOPTOTIC NEURODEGENERATION IN PRENATAL RAT HIPPOCAMPAL NEURONS

Naseer MI, Ullah N, Ullah I, Koh PO, Lee HY, Park MS, Kim MO.
Division of Life Science, College of Natural Sciences (RINS) and Applied Life Science (BK 21).

ABSTRACT
Exposure to alcohol during brain development may cause a neurological syndrome called fetal alcohol syndrome (FAS), characterized by pre- and postnatal growth deficiencies, craniofacial anomalies and evidence of CNS dysfunction. The objective of this study was to evaluate pentylenetetrazol (PTZ) and ethanol effects on Bax, Bcl-2 expression, which further induced activation of caspase-3, release of cytochrome-c from mitochondria and to observe the protective effects of vitamin C (vit-C) against PTZ and ethanol-induced apoptotic neurodegeneration in primary cultured neuronal cells at gestational day (GD) 17.5. Apoptotic neurodegeneration and neuroprotective effect of vit-C was measured by using MTT assay, Western blot analysis which further conformed by measurement of mitochondrial membrane potential using JC-1 detection kit and immunofluorescence analysis. The results showed that PTZ and ethanol produced extensive Bax-dependent caspase-9, caspase-3 activation and caused neuronal apoptosis. Furthermore, the co treatment of vit-C along with ethanol and PTZ showed significantly decreased expression of Bax, caspase-9, caspase-3, cytochrome-c and significantly increased expression of anti-apoptotic Bcl-2 protein as compared to control group. Our findings indicate that PTZ and ethanol activates an intrinsic apoptotic death program in neurons that is likely to contribute to the neuropathologic effects in fetal alcohol exposure and vit-C can prevent some of the deleterious effects of PTZ and ethanol on the developing brain. The available experimental evidence and the safety of vit-C in pregnancy suggest that experimental use of ascorbic acid as a new and effective protective agent ethanol and PTZ induced apoptotic neurodegeneration.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20963815

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PubMed, Alcohol Clin Exp Res. 2010 Oct 19. doi: 10.1111/j.1530-0277.2010.01323.x.

2) THE EFFECTS OF MATERNAL BINGE DRINKING DURING PREGNANCY ON NEURAL CORRELATES OF RESPONSE INHIBITION AND MEMORY IN CHILDHOOD

Burden MJ, Westerlund A, Muckle G, Dodge N, Dewailly E, Nelson CA, Jacobson SW, Jacobson JL.
From the Department of Psychiatry and Behavioral Neurosciences (MJB, ND, SWJ, JLJ), Wayne State University School of Medicine, Detroit, Michigan; Children's Hospital Boston (AW, CAN), Harvard Medical School, Boston, Massachusetts; and Laval University (GM, ED), Quebec, Canada.

ABSTRACT
Background: Although an extensive literature has documented a broad range of cognitive performance deficits in children with prenatal alcohol exposure, little is known about how the neurophysiological processes underlying these deficits may be affected. Event-related potentials (ERPs), which reflect task-specific changes in brain electrical activity, provide a method for examining multiple constituents of cognitive processing at the neural level.
Methods: We recorded ERPs in 217 children from Inuit communities in Arctic Quebec (M age = 11.3 years) during 2 different tasks-Go/No-go response inhibition and continuous recognition

memory. Children were classified as either alcohol-exposed (ALC) or controls (CON) depending on whether the mother reported binge drinking during pregnancy.

Results: Both groups performed comparably in terms of accuracy and reaction time on the tasks, and both tasks elicited the expected effects on ERPs when responses were compared across conditions. However, the ALC group showed slower P2 latencies on Go/No-go, suggesting an altered neurophysiological response associated with initial visual processing of the stimuli. On the memory task, the ALC group showed reduced FN400 amplitude to New items, known as the familiarity effect, and reduced amplitude for the late positive component, possibly reflecting impairment in memory retrieval.

Conclusions: These findings show that, even in tasks in which alcohol-exposed children exhibit behavioral performance that is comparable to controls, fetal alcohol exposure is associated with altered neurophysiological processing of response inhibition and recognition memory. The data suggest that fetal alcohol exposure is associated with reduced efficiency in the initial extracting of the meaning of a stimulus, reduced allocation of attention to the task, and poorer conscious, explicit recognition memory processing.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20958332

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PubMed, Alcohol Clin Exp Res. 2010 Oct 19. doi: 10.1111/j.1530-0277.2010.01318.x. [Epub ahead of print]

3) UPREGULATION OF CANNABINOID TYPE 1 RECEPTORS IN DOPAMINE D2 RECEPTOR KNOCKOUT MICE IS REVERSED BY CHRONIC FORCED ETHANOL CONSUMPTION

Thanos PK, Gopez V, Delis F, Michaelides M, Grandy DK, Wang GJ, Kunos G, Volkow ND.

From the Department of Health and Human Services (PKT, NDV), Laboratory of Neuroimaging, NIAAA, NIH, Bethesda, Maryland; Department of Medicine (PKT, VG, FD, MM, GJW), Behavioral Neuropharmacology & Neuroimaging Lab, Brookhaven National Laboratory, Upton, New York; Department of Psychology (MM), SUNY Stony Brook, Stony Brook, New York; Department of Physiology and Pharmacology (DKG), Oregon Health and Science University, Portland, Oregon; and Department of Health and Human Services (GK), Laboratory of Physiologic Studies, NIAAA, NIH, Bethesda, Maryland.

ABSTRACT

Background: The anatomical proximity of the cannabinoid type 1 (CNR1/CB1R) and the dopamine D2 receptors (DRD2), their ability to form CB1R-DRD2 heteromers, their opposing roles in locomotion, and their involvement in ethanol's reinforcing and addictive properties prompted us to study the levels and distribution of CB1R after chronic ethanol intake, in the presence and absence of DRD2.

Methods: We monitored the drinking patterns and locomotor activity of Drd2+/+ and Drd2-/- mice consuming either water or a 20% (v/v) ethanol solution (forced ethanol intake) for 6 months and used the selective CB1 receptor antagonist [(3) H]SR141716A to quantify CB1R levels in different brain regions with in vitro receptor autoradiography.

Results: We found that the lack of DRD2 leads to a marked upregulation (approximately 2-fold increase) of CB1R in the cerebral cortex, the caudate-putamen, and the nucleus accumbens, which was reversed by chronic ethanol intake.

Conclusions: The results suggest that DRD2-mediated dopaminergic neurotransmission and chronic ethanol intake exert an inhibitory effect on cannabinoid receptor expression in cortical and striatal regions implicated in the reinforcing and addictive properties of ethanol.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20958329

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PubMed, Am J Med Genet A. 2010 Oct 14. [Epub ahead of print]

4) FETAL ALCOHOL SPECTRUM DISORDERS: EXTENDING THE RANGE OF STRUCTURAL DEFECTS

Jones KL, Hoyme HE, Robinson LK, Del Campo M, Manning MA, Prewitt LM, Chambers CD.
Department of Pediatrics, University of California, San Diego and Rady Children's Hospital, San Diego, California.

ABSTRACT
Although the structural phenotype of fetal alcohol syndrome (FAS) is established, prenatal exposure to alcohol may produce a broader spectrum of defects, fetal alcohol spectrum disorder (FASD). Documenting the full spectrum of defects associated with FASD is critical to determining the true incidence of this disorder. We examined 831 children from the Collaborative Initiative on Fetal Alcohol Spectrum Disorders using a structured protocol for diagnosis of FAS using the cardinal facial and growth features, and assessment of additional structural defects thought to occur more often in children with prenatal alcohol exposure. Subjects were classified as FAS, Deferred (some characteristic features of FAS), or No FAS, Groups were compared on prevalence of additional features and number of additional features observed, stratified by diagnostic category, sex, race, and age. Prevalence of most additional features was greatest among subjects with FAS and least among No FAS. A higher frequency of additional features was observed among FAS and Deferred subjects ≥12 years of age than among those under 12. FAS and Deferred Whites had greater frequency of additional features than Cape Colored. Prenatal alcohol exposure may produce a broad spectrum of structural defects that goes beyond FAS with implications regarding the impact of alcohol on the developing fetus, a prerequisite for ultimate prevention of FASD.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20949507

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PubMed, Cerebellum. 2010 Oct 7. [Epub ahead of print]

5) MECHANISMS OF ETHANOL-INDUCED DEATH OF CEREBELLAR GRANULE CELLS

Luo J.
Department of Internal Medicine, University of Kentucky College of Medicine, 130 Bosomworth Health Sciences Research Building, 1095 Veterans Drive, Lexington, KY, 40536, USA, jialuo888@uky.edu.

ABSTRACT
Maternal ethanol exposure during pregnancy may cause fetal alcohol spectrum disorders (FASD). FASD is the leading cause of mental retardation. The most deleterious effect of fetal alcohol exposure

is inducing neuroapoptosis in the developing brain. Ethanol-induced loss of neurons in the central nervous system underlies many of the behavioral deficits observed in FASD. The cerebellum is one of the brain areas that are most susceptible to ethanol during development. Ethanol exposure causes a loss of both cerebellar Purkinje cells and granule cells. This review focuses on the toxic effect of ethanol on cerebellar granule cells (CGC) and the underlying mechanisms. Both in vitro and in vivo studies indicate that ethanol induces apoptotic death of CGC. The vulnerability of CGC to ethanol-induced death diminishes over time as neurons mature. Several mechanisms for ethanol-induced apoptosis of CGC have been suggested. These include inhibition of N-methyl-D: -aspartate receptors, interference with signaling by neurotrophic factors, induction of oxidative stress, modulation of retinoid acid signaling, disturbance of potassium channel currents, thiamine deficiency, and disruption of translational regulation. Cultures of CGC provide an excellent system to investigate cellular/molecular mechanisms of ethanol-induced neurodegeneration and to evaluate interventional strategies. This review will also discuss the approaches leading to neuroprotection against ethanol-induced neuroapoptosis.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20927663?dopt=Abstract

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Liebertonline, Telemedicine and e-Health. Online Ahead of Print: October 6, 2010.

6) USING TELEHEALTH FOR ASSESSMENT OF FETAL ALCOHOL SPECTRUM DISORDER: THE EXPERIENCE OF TWO CANADIAN RURAL AND REMOTE COMMUNITIES

Carla D.L. Ens, Ph.D.,[1,2,] Ana Hanlon-Dearman, M.D.,[1,3,] Mary Cox Millar, B.A.,[1,3] and Sally Longstaffe, M.D.[1]
[1] Manitoba FASD Centre, Winnipeg, Manitoba, Canada.
[2] Department of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada.
[3] Departmentof Pediatrics and Child Health, Faculty of Medicine, University of Manitoba, Winnipeg, Manitoba, Canada.

ABSTRACT
Introduction: Telehealth has been used for fetal alcohol spectrum disorder (FASD) diagnostic assessment in select Manitoban communities since 2000.

Objective: The purpose of this study was to evaluate the FASD telehealth program within two rural and remote Northern Manitoban communities by comparing community practices from the perspective of professionals working with the FASD diagnostic clinics in these communities. Recommendations for the further development of FASD assessment by telehealth were made to further improve current implementation and guide expansion of the FASD telehealth program within the province. Methodology: Semistructured interviews were conducted from October 19 to December 11, 2009. Participants (N=26) were comprised of professionals, including those in the education, social services, and health sectors.

Results and Recommendations: Two themes emerged from the data and covered the perceived strengths and drawbacks with the program, and meaningful suggestions to improve the service. Participants regarded the FASD telehealth program as successful and useful, especially given the remote location of the communities and the lack of on-site services. Recommendations addressing the barriers pertaining to the process were made from the study's findings and available scientific literature.

Conclusions: This study will provide a solid basis for the successful further development of the FASD telehealth programs.

Read Full Article,
http://www.liebertonline.com/doi/abs/10.1089/tmj.2010.0070

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PubMed, J Epidemiol Community Health. 2010 Oct 5. [Epub ahead of print]

7) LIGHT DRINKING DURING PREGNANCY: STILL NO INCREASED RISK FOR SOCIOEMOTIONAL DIFFICULTIES OR COGNITIVE DEFICITS AT 5 YEARS OF AGE?

Kelly YJ, Sacker A, Gray R, Kelly J, Wolke D, Head J, Quigley MA.
University College London, London, UK.

ABSTRACT
Background: This study examines the relationship between light drinking during pregnancy and the risk of socioemotional problems and cognitive deficits at age 5 years.

Methods: Data from the nationally representative prospective UK Millennium Cohort Study (N=11 513) were used. Participants were grouped according to mothers' reported alcohol consumption during pregnancy: never drinker; not in pregnancy; light; moderate; heavy/binge. At age 5 years the strengths and difficulties questionnaire (SDQ) and British ability scales (BAS) tests were administered during home interviews. Defined clinically relevant cut-offs on the SDQ and standardised scores for the BAS subscales were used.

Results: Boys and girls born to light drinkers were less likely to have high total difficulties (for boys 6.6% vs 9.6%, OR=0.67, for girls 4.3% vs 6.2%, OR=0.69) and hyperactivity (for boys 10.1% vs 13.4%, OR=0.73, for girls 5.5% vs 7.6%, OR=0.71) scores compared with those born to mothers in the not-in-pregnancy group. These differences were attenuated on adjustment for confounding and mediating factors. Boys and girls born to light drinkers had higher mean cognitive test scores compared with those born to mothers in the not-in-pregnancy group: for boys, naming vocabulary (58 vs 55), picture similarities (56 vs 55) and pattern construction (52 vs 50), for girls naming vocabulary (58 vs 56) and pattern construction (53 vs 52). Differences remained statistically significant for boys in naming vocabulary and picture similarities.

Conclusions: At age 5 years cohort members born to mothers who drank up to 1–2 drinks per week or per occasion during pregnancy were not at increased risk of clinically relevant behavioural difficulties or cognitive deficits compared with children of mothers in the not-in-pregnancy group.

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PubMed, Birth Defects Res A Clin Mol Teratol. 2010 Oct 1. [Epub ahead of print]

8) ASSESSMENT OF BENEFITS OF A UNIVERSAL SCREEN FOR MATERNAL ALCOHOL USE DURING PREGNANCY

Gifford AE, Farkas KJ, Jackson LW, Molteno CD, Jacobson JL, Jacobson SW, Bearer CF.
International Society for Disease Surveillance, Boston, Massachusetts.

ABSTRACT
Introduction: The objective of this report is to estimate the benefits of universal meconium screening for maternal drinking during pregnancy. Fetal alcohol spectrum disorder (FASD), including its most

severe manifestation fetal alcohol syndrome (FAS), is preventable and remains a public health tragedy. The incidences of FAS and FASD have been conservatively estimated to be 0.97 and 10 per 1000 births, respectively. Meconium testing has been demonstrated to be a promising at-birth method for detection of drinking during pregnancy.

Methods: The current costs of FAS and FASD, alcohol treatment programs, and meconium screening were estimated by literature review. Monetary values were converted roughly to equal dollars in 2006.

Results: Costs of adding meconium analysis to the current newborn screening program and of treatment for the identified mothers were estimated and compared to potential averted costs that may result from identification and intervention for mothers and affected infants. Three potential maternal treatment strategies are analyzed. Depending on the treatment type, the savings may range from $6 to $97 for every $1 spent on screening and treatment.

Discussion: It needs to be emphasized, however, that such screening is premature and that to be effective this screening can be implemented only if there is a societal willingness to institute prevention and intervention programs to improve both women's and children's health. Future research should be directed at improving detection and developing in-depth prevention and remedial intervention programs. A thorough consideration of the ethical issues involved in such a screening program is also needed. Birth Defects Research (Part A), 2010.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20890939

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PubMed, Clin Chim Acta. 2010 Oct 1. [Epub ahead of print]

9) CHANGES IN TRANSFERRIN GLYCOSYLATION DURING PREGNANCY MAY LEAD TO FALSE-POSITIVE CARBOHYDRATE-DEFICIENT TRANSFERRIN (CDT) RESULTS IN TESTING FOR RISKFUL ALCOHOL CONSUMPTION

Kenan N, Larsson A, Axelsson O, Helander A.
Alcohol Laboratory, Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden.

ABSTRACT

Background: An alcohol-induced change in serum transferrin glycosylation, termed carbohydrate-deficient transferrin (CDT), is widely used as a biomarker of heavy long-term drinking. This study examined the transferrin glycosylation profile and the risk for false-positive CDT results during pregnancy.

Methods: Serum samples were collected from 24 healthy pregnant women starting in gestation week 9-21, throughout pregnancy, and 8 or more weeks after delivery. Altogether 171 sera (5-9 samples/person) were analysed. Transferrin glycoforms were quantified as a percentage of total transferrin, using an HPLC candidate reference method for CDT.

Results: During pregnancy, the relative disialo-, pentasialo- and hexasialotransferrin levels increased gradually, whereas trisialo- and tetrasialotransferrin were reduced. This effect was most pronounced in the third trimester. For disialotransferrin, the main target in CDT testing, initial values of 1.07±0.17% (mean±SD) increased to 1.61±0.23% before delivery (~50% increase). Nine (38%) pregnant women reached %disialotransferrin values ≥1.7% (97.5th percentile for controls) but all results were <2.0%. In the postpartum samples, all glycoform levels had returned towards the starting values.

Conclusions: These results suggest that the cutoff for %disialotransferrin and %CDT employed to indicate heavy long-term drinking need to be raised slightly in pregnant women, to minimize the risk for false-positive results on CDT testing.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20869959

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PubMed, Obstet Gynecol. 2010 Oct;116(4):827-33.

10) SCREENING FOR PRENATAL SUBSTANCE USE: DEVELOPMENT OF THE SUBSTANCE USE RISK PROFILE-PREGNANCY SCALE

Yonkers KA, Gotman N, Kershaw T, Forray A, Howell HB, Rounsaville BJ.
Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut, USA. Kimberly.Yonkers@yale.edu

ABSTRACT
Objective: To report on the development of a questionnaire to screen for hazardous substance use in pregnant women and to compare the performance of the questionnaire with other drug and alcohol measures.

Methods: Pregnant women were administered a modified TWEAK (Tolerance, Worried, Eye-openers, Amnesia, K[C] Cut Down) questionnaire, the 4Ps Plus questionnaire, items from the Addiction Severity Index, and two questions about domestic violence (N=2,684). The sample was divided into "training" (n=1,610) and "validation" (n=1,074) subsamples. We applied recursive partitioning class analysis to the responses from individuals in the training subsample that resulted in a three-item Substance Use Risk Profile-Pregnancy scale. We examined sensitivity, specificity, and the fit of logistic regression models in the validation subsample to compare the performance of the Substance Use Risk Profile-Pregnancy scale with the modified TWEAK and various scoring algorithms of the 4Ps.

Results: The Substance Use Risk Profile-Pregnancy scale is comprised of three informative questions that can be scored for high- or low-risk populations. The Substance Use Risk Profile-Pregnancy scale algorithm for low-risk populations was mostly highly predictive of substance use in the validation subsample (Akaike's Information Criterion=579.75, Nagelkerke R=0.27) with high sensitivity (91%) and adequate specificity (67%). The high-risk algorithm had lower sensitivity (57%) but higher specificity (88%).

Conclusion: The Substance Use Risk Profile-Pregnancy scale is simple and flexible with good sensitivity and specificity. The Substance Use Risk Profile-Pregnancy scale can potentially detect a range of substances that may be abused. Clinicians need to further assess women with a positive screen to identify those who require treatment for alcohol or illicit substance use in pregnancy.

Level Of Evidence: III.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20859145

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American Association on Intellectual and Developmental Disabilities, October 2010

11) CHILDREN AND YOUTH WITH FETAL ALCOHOL SPECTRUM DISORDERS: SUMMARY OF INTERVENTION RECOMMENDATIONS AFTER CLINICAL DIAGNOSIS

Tracy Jirikowic, Julie Gelo, and Susan Astley

ABSTRACT

Children with fetal alcohol spectrum disorders (FASDs) present with a wide range of developmental disabilities; however, clinical standards of care after a diagnosis are not well established. This retrospective review summarizes the types of intervention recommendations generated by an interdisciplinary FASD diagnostic team for 120 children ages 0.2 to 16.5 years receiving an FASD diagnosis at the University of Washington FAS Diagnostic & Prevention Network Clinic. Intervention recommendations documented in a FASD diagnostic summary report and submitted to each patient's medical record were subject to masked review and content analysis. Intervention recommendations were compared across 3 FASD diagnostic groups and selected demographic variables. The results show the type and frequency of services, supports, and resources recommended to a clinical sample of children with FASD.

Read Full Article,
http://www.aaiddjournals.org/doi/abs/10.1352/1934-9556-48.5.330

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PubMed, Clin Dysmorphol. 2010 Oct;19(4):175-80.

12) FETAL ALCOHOL SYNDROME: A PHENOCOPY OF SPONDYLOCARPOTARSAL SYNOSTOSIS SYNDROME?

Vassel J, Rupps R, Krakow D, Puvanachandra N, Gardiner JA, Lazeo SR, Boerkoel CF.
Rare Disease Foundation, Vancouver, BC, Canada.

No abstract Available

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20717009

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Wiley, Developmental Psychobiology. Volume 52, Issue 7, pages 625–637, November 2010. First Published Online: 29th September 2010

13) CHALLENGES TO MATERNAL WELLBEING DURING PREGNANCY IMPACT TEMPERAMENT, ATTENTION, AND NEUROMOTOR RESPONSES IN THE INFANT RHESUS MONKEY

Christopher L. Coe[1], Gabriele R. Lubach[1], Heather R. Crispen[1], Elizabeth A. Shirtcliff[2], Mary L. Schneider[3]
[1] Harlow Center for Biological Psychology, University of Wisconsin, 22 N. Charter Street, Madison, WI 53715.
[2] Department of Psychology, University of New Orleans, New Orleans, LA.
[3] Department of Kinesiology, University of Wisconsin, Madison, WI.

ABSTRACT

The relative maturity, alertness, and reactivity of an infant at birth are sensitive indices of the neonate's health, the quality of the pregnancy, and the mother's wellbeing. Even when fetal growth and gestation

length have been normal, the maturing fetus can still be adversely impacted by both physical events and psychological challenges to the mother during the prenatal period. The following research evaluated 413 rhesus monkeys from 7 different types of pregnancies to determine which conditions significantly influenced the behavioral responsiveness and state of the young infant. A standardized test battery modeled after the Neonatal Behavioral Assessment Scale for human newborns was employed. The largest impairments in orientation and increases in infant emotional reactivity were seen when female monkeys drank alcohol, even though consumed at only moderate levels during part of the pregnancy. The infants' ability to focus and attend to visual and auditory cues was also affected when the gravid female's adrenal hormones were transiently elevated for 2 weeks by ACTH administration. In addition, responses to tactile and vestibular stimulation were altered by both this ACTH treatment and psychological disturbance during gestation. Conversely, a 2-day course of antenatal corticosteroids 1 month before term resulted in infants with lower motor activity and reactivity.

These findings highlight several pregnancy conditions that can affect a young infant's neurobehavioral status, even when otherwise healthy, and demonstrate that alterations or deficits are specific to the type of insult experienced by the mother and fetus.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1002/dev.20489/abstract

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UnboundMedLine, Int J Law Psychiatry 2010 Sep 29.

14) TRYING DIFFERENTLY: A RELATIONSHIP-CENTERED APPROACH TO REPRESENTING CLIENTS WITH COGNITIVE CHALLENGES

Boulding DM, Brooks SL
Port Coquitlam, B.C., Canada.

ABSTRACT
This article demonstrates the usefulness of an innovative framework called "Relationship-Centered Lawyering" to enhancing real world legal practice. It uses the example of lawyers, particularly criminal defense lawyers, who often deal with clients with cognitive challenges. The article developed out of a series of workshops conducted jointly by the co-authors, an American law professor with a social work background, and a Canadian criminal defense lawyer and family mediator who is an international expert on Fetal Alcohol Spectrum Disorder and other Neuro-Behavioral Disorders (FA/NB). The paper describes the relational theory Brooks developed (along with Robert Madden), along with the science of cognitive impairments, with a specific focus on FA/NB. The paper provides two illustrations of the relational framework by explaining Boulding's strategy of creating what is called the "external brain" and his techniques of relational interviewing.

Link to the Article,
http://www.unboundmedicine.com/medline/ebm/record/20888044/abstract/Trying_differently:_A_relationship_centered_approach_to_representing_clients_with_cognitive_challenges_

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PubMed, Birth Defects Res A Clin Mol Teratol. 2010 Sep 28. [Epub ahead of print]

15) POSTNATAL GROWTH RESTRICTION AND GENE EXPRESSION CHANGES IN A MOUSE MODEL OF FETAL ALCOHOL SYNDROME

Kaminen-Ahola N, Ahola A, Flatscher-Bader T, Wilkins SJ, Anderson GJ, Whitelaw E, Chong S.
Epigenetics Laboratory, Queensland Institute of Medical Research, Herston, Australia.

ABSTRACT

Growth restriction, craniofacial dysmorphology, and central nervous system defects are the main diagnostic features of fetal alcohol syndrome. Studies in humans and mice have reported that the growth restriction can be prenatal or postnatal, but the underlying mechanisms remain unknown.We recently described a mouse model of moderate gestational ethanol exposure that produces measurable phenotypes in line with fetal alcohol syndrome (e.g., craniofacial changes and growth restriction in adolescent mice). In this study, we characterize in detail the growth restriction phenotype by measuring body weight at gestational day 16.5, cross-fostering from birth to weaning, and by extending our observations into adulthood. Furthermore, in an attempt to unravel the molecular events contributing to the growth phenotype, we have compared gene expression patterns in the liver and kidney of nonfostered, ethanol-exposed and control mice at postnatal day 28.We find that the ethanol-induced growth phenotype is not detectable prior to birth, but is present at weaning, even in mice that have been cross-fostered to unexposed dams. This finding suggests a postnatal growth restriction phenotype that is not due to deficient postpartum care by dams that drank ethanol, but rather a physiologic result of ethanol exposure in utero. We also find that, despite some catch-up growth after 5 weeks of age, the effect extends into adulthood, which is consistent with longitudinal studies in humans.Genome-wide gene expression analysis revealed interesting ethanol-induced changes in the liver, including genes involved in the metabolism of exogenous and endogenous compounds, iron homeostasis, and lipid metabolism. Birth Defects Research (Part A), 2010.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20878912

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PubMed, Pediatrics. 2010 Oct;126(4):e843-50. Epub 2010 Sep 27.

16) PRENATAL ALCOHOL EXPOSURE AND RISK OF BIRTH DEFECTS

O'Leary CM, Nassar N, Kurinczuk JJ, de Klerk N, Geelhoed E, Elliott EJ, Bower C.
Telethon Institute for Child Health Research, Centre for Child Health Research, Department of Health Economics, School of Population Health, University of Western Australia, PO Box 855, West Perth, WA 6872, Australia. colleeno@ichr.uwa.edu.au

ABSTRACT

Objective: The goal was to examine the associations between dose, pattern, and timing of prenatal alcohol exposure (PAE) and birth defects.

Methods: Data from a randomly selected, population-based cohort of nonindigenous women who gave birth to a live infant in Western Australia (WA) between 1995 and 1997 (N=4714) were linked to WA Midwives Notification System and WA Birth Defects Registry data. We assessed the associations of PAE before pregnancy, in the first trimester, and in late pregnancy with any birth defect and with birth defects classified as alcohol-related birth defects (ARBDs) by the Institute of Medicine (IOM), by using logistic regression.

Results: The prevalence of birth defects classified as ARBDs by the IOM was low. Compared with abstinence, heavy PAE in the first trimester was associated with increased odds of birth defects classified as ARBDs (adjusted odds ratio: 4.6 [95% confidence interval: 1.5-14.3]), with similar findings after validation through bootstrap analysis. There was no association between low or moderate PAE and birth defects.

Conclusions: A fourfold increased risk of birth defects classified as ARBDs was observed after heavy PAE in the first trimester. Many individual birth defects included in the IOM classification for ARBDs either were not present in this cohort or were not associated with PAE. Large, population-based studies are needed to strengthen the evidence base for ARBDs.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20876169

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Wiley, Child: Care, Health and Development. Early view. Article first published online: 21 SEP 2010.

17) An evaluation of social skills in children with and without prenatal alcohol exposure

C. Rasmussen[1], M. Becker[2], J. McLennan[3], L. Urichuk[4], G. Andrew[5].
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[2] University of Alberta, Edmonton.
[3] Department of Community Health Sciences and Psychiatry, Department of Pediatrics, Department of Psychology, University of Calgary, Calgary.
[4] Child and Adolescent Services Association (CASA), Education, Planning, Research and Evaluation Regional Mental Health Program, Alberta Health Services – Capital Health, Department of Psychiatry, University of Alberta.
[5] Alberta Health Services – Capital Health, Department of Pediatrics, University of Alberta, Edmonton, B, Canada.

ABSTRACT
Background: The goal of this study was to examine social skills deficits among children with and without prenatal alcohol exposure (PAE) who were both referred to a respite programme.

Methods: Thirty-seven children with PAE and 23 non-exposed children (aged 3 to 8 years) were evaluated on the Social Skills Rating System (SSRS) by their caregivers and respite workers.

Results: As compared with the non-exposed children, those with PAE showed more deficits on caregiver ratings of responsibility, hyperactivity, internalizing problems and overall social skills, as well as respite worker ratings of hyperactivity. The social skills among the PAE group were not related to home placement variables. Among both groups, caregivers rated social skills lower than respite workers, and among the PAE group, girls tended to display more social skills deficits than boys.

Conclusions: The SSRS is useful in identifying unique social skills deficits among children with PAE.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2214.2010.01152.x/abstract

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Karger, Hormone Research in Paediatrics. 2010 Sep 15

18) EFFECTS OF PRENATAL ETHANOL EXPOSURE ON POSTNATAL GROWTH AND THE INSULIN-LIKE GROWTH FACTOR AXIS

Sofía Aros[a], James L. Millsc, Germán Iñiguez[b], Alejandra Avila[b], Mary R. Conley[c], James Troendle[c], Christopher Cox[c], Fernando Cassorla[b]
a Department of Pediatrics, Faculty of Medicine, University of Chile, San Borja Arriarán Clinical Hospital, and
b Institute of Maternal and Child Research, Faculty of Medicine, University of Chile, Santiago, Chile;
c Division of Epidemiology, Statistics and Prevention Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Department of Health and Human Services, Bethesda, Md., USA

ABSTRACT
Aims: To study the effect of in-utero alcohol exposure on the insulin-like growth factor axis (IGF) and leptin during infancy and childhood, considering that exposed children may exhibit pre- and postnatal growth retardation.

Methods: We prospectively identified heavily drinking pregnant women who consumed on average 4 or more drinks of ethanol per day (≥48 g/day) and assessed growth in 69 of their offspring and an unexposed control group of 83 children, measuring serum IGF-I (radioimmunoassay), IGF-II (immunoradiometric assay, IRMA), insulin-like growth factor-binding protein 3 (IGFBP-3) (IRMA) and leptin (IRMA) at 1 month and 1, 2, 3, 4, and 5 years of age.

Results: IGF-II levels increased with age in both groups, but the rate of increase was significantly higher in exposed children, and levels were significantly higher in ethanol-exposed children at 3, 4, and 5 years of age. In exposed children, IGF-I levels were higher at 3 and 4 years and leptin levels were significantly lower at 1 and 2 years. Exposed subjects showed a much lower correlation between IGF-I and growth parameters than unexposed subjects.

Conclusion: Exposure to ethanol during pregnancy increases IGF-I and IGF-II and decreases leptin during early childhood. The increase in serum IGF-II concentrations in ethanol-exposed children suggests that this hormone should be explored as a potential marker for prenatal alcohol exposure.

Read Full Article,
http://content.karger.com/ProdukteDB/produkte.asp?Aktion=ShowFulltext&ArtikelNr=319706&Ausgabe=0&ProduktNr=224036

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PubMed, Birth Defects Res A Clin Mol Teratol. 2010 Sep 14. [Epub ahead of print]

19) MAGNETIC RESONANCE MICROSCOPY-BASED ANALYSES OF THE BRAINS OF NORMAL AND ETHANOL-EXPOSED FETAL MICE

O'Leary-Moore SK, Parnell SE, Godin EA, Dehart DB, Ament JJ, Khan AA, Johnson GA, Styner MA, Sulik KK.
Bowles Center for Alcohol Studies, University of North Carolina, Chapel Hill, North Carolina.

ABSTRACT
Background: The application of magnetic resonance microscopy (MRM) to the study of normal and abnormal prenatal mouse development has facilitated discovery of dysmorphology following prenatal ethanol insult. The current analyses extend this work, providing a regional brain volume-based

description of normal braingrowth and illustrating the consequences of gestational day (GD) 10 ethanol exposure in the fetal mouse.

Methods: To assess normal growth, control C57Bl/6J fetuses collected on GD 16, GD 16.5, and GD 17 were scanned using a 9.4-T magnet, resulting in 29-μm isotropic resolution images. For the ethanol teratogenicity studies, C57Bl/6J dams were administered intraperitoneal ethanol (2.9 g/kg) at 10 days, 0 hr, and 10 days, 4 hr, after fertilization, and fetuses were collected for analyses on GD 17. From individual MRM scans, linear measurements and regional brain volumes were determined and compared.

Results: In control fetuses, each of the assessed brain regions increased in volume, whereas ventricular volumes decreased between GD 16 and GD 17. Illustrating a global developmental delay, prenatal ethanol exposure resulted in reduced body volumes, crown-rump lengths, and a generalized decrease in regional brain volumes compared with GD 17 controls. However, compared with GD 16.5, morphologically matched controls, ethanol exposure resulted in volume increases in the lateral and third ventricles as well as a disproportionate reduction in cortical volume.

Conclusions: The normative data collected in this study facilitate the distinction between GD 10 ethanol-induced developmental delay and frank dysmorphology. This work illustrates the utility of MRM-based analyses for developmental toxicology studies and extends our knowledge of the stage-dependency of ethanol teratogenesis.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20842647

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PubMed, J Am Soc Nephrol. 2010 Sep 9. [Epub ahead of print]

20) PRENATAL EXPOSURE TO ALCOHOL REDUCES NEPHRON NUMBER AND RAISES BLOOD PRESSURE IN PROGENY

Gray SP, Denton KM, Cullen-McEwen L, Bertram JF, Moritz KM.
Departments of *Anatomy and Developmental Biology and.

ABSTRACT
Prenatal ethanol exposure is teratogenic, but the effects of ethanol on kidney development and the health of offspring are incompletely understood. Our objective was to investigate the effects of acute ethanol exposure during pregnancy on nephron endowment, mean arterial pressure, and renal function in offspring. We administered ethanol or saline by gavage to pregnant Sprague-Dawley rats on embryonic days 13.5 and 14.5. At 1 month of age, the nephron number was 15% lower and 10% lower in ethanol-exposed males and females, respectively, compared with controls. Mean arterial pressure, measured in conscious animals via indwelling tail-artery catheter, was 10% higher in both ethanol-exposed males and females compared with controls. GFR was 20% higher in ethanol-exposed males but 15% lower in ethanol-exposed females; moreover, males had increased proteinuria compared with controls. Furthermore, embryonic kidneys cultured in the presence of ethanol for 48 hours had 15% fewer ureteric branch points and tips than kidneys cultured in control media. Taken together, these data demonstrate that acute prenatal ethanol exposure reduces the number of nephrons, possibly as a result of inhibited ureteric branching morphogenesis, and that these changes affect adult cardiovascular and renal function.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20829403

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PubMed, Neuropsychiatr Dis Treat. 2010 Sep 7;6:509-15.

21) DISTINGUISHING BETWEEN ATTENTION-DEFICIT HYPERACTIVITY AND FETAL ALCOHOL SPECTRUM DISORDERS IN CHILDREN: CLINICAL GUIDELINES

Peadon E, Elliott EJ.
Discipline of Paediatrics and Child, Health, Sydney Medical School, University of Sydney, Sydney, Australia.

ABSTRACT

Fetal alcohol spectrum disorders (FASD) are the physical and neurodevelopmental outcomes of fetal alcohol exposure. The behavioral phenotype of children with FASD includes difficulties with executive function, memory, planning, processing speed, and attention. Although attention deficit hyperactivity disorder (ADHD) is diagnosed in up to 94% of individuals with heavy prenatal alcohol exposure, the exact relationship between FASD and ADHD is unclear. There is some evidence that ADHD in FASD may be a specific clinical subtype and thus may require a different treatment approach. Although traditional behavioral observation scales may not distinguish between the two groups, there is evidence that children with FASD have a different profile on the four-factor model of attention than children with ADHD who do not have FASD. There is a paucity of good scientific evidence on effective interventions for individuals with ADHD and FASD. There is weak evidence that children with FASD and ADHD may have a better response to dexamphetamine than methylphenidate. There is a strong need for larger, high quality studies to examine the relationship between ADHD and FASD and identify effective treatments because management of inattention and hyperactivity may improve learning and ameliorate the common secondary disabilities associated with FASD.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20856914

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PubMed, Subst Abuse Treat Prev Policy. 2010 Sep 6;5:22.

22) PSYCHOLOGICAL DISTRESS AMONG PLAINS INDIAN MOTHERS WITH CHILDREN REFERRED TO SCREENING FOR FETAL ALCOHOL SPECTRUM DISORDERS

Parker T, Maviglia MA, Lewis PT, Phillip Gossage J, May PA.
Department of Family and Community Medicine, University of New Mexico School of Medicine, MSC09 5040, 1 University of New Mexico, Albuquerque, New Mexico, USA.

ABSTRACT

Background: Psychological distress (PD) includes symptoms of depression and anxiety and is associated with considerable emotional suffering, social dysfunction and, often, with problematic alcohol use. The rate of current PD among American Indian women is approximately 2.5 times higher than that of U.S. women in general. Our study aims to fill the current knowledge gap about the prevalence and characteristics of PD and its association with self-reported current drinking problems among American Indian mothers whose children were referred to screening for fetal alcohol spectrum disorders (FASD).

Methods: Secondary analysis of cross-sectional data was conducted from maternal interviews of referred American Indian mothers (n = 152) and a comparison group of mothers (n = 33) from the same Plains culture tribes who participated in an NIAAA-funded epidemiology study of FASD. Referred women were from one of six Plains Indian reservation communities and one urban area who bore children suspected of having an FASD. A 6-item PD scale (PD-6, Cronbach's alpha = .86) was

constructed with a summed score range of 0-12 and a cut-point of 7 indicating serious PD. Multiple statistical tests were used to examine the characteristics of PD and its association with self-reported current drinking problems.

Results: Referred and comparison mothers had an average age of 31.3 years but differed (respectively) on: education (<high school: 47.4%, 9.1%), PD-6 mean scores (3.57, 1.48), current prevalence of serious PD (19.1%, 0.0%), and a current drinking problem (31.6%, 12.1%). Among referred mothers, those with a current drinking problem had a significantly higher mean PD-6 score. Having PD, serious PD, and 2 specific scale items significantly increased the odds that a referred mother would have a current drinking problem.

Conclusions: Psychological distress among referred mothers is significantly associated with having a self-reported drinking problem. FASD prevention requires multi-level prevention efforts that provide real opportunities for educational attainment and screening and monitoring of PD and alcohol use during the childbearing years. Mixed methods studies are needed to illuminate the social and cultural determinants at the base of the experience of PD and to identify the strengths and protective factors of unaffected peers who reside within the same communities.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20819208

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PubMed, Am J Epidemiol. 2010 Oct 15;172(8):924-31. Epub 2010 Sep 1.

23) MATERNAL ALCOHOL CONSUMPTION, ALCOHOL METABOLISM GENES, AND THE RISK OF ORAL CLEFTS: A POPULATION-BASED CASE-CONTROL STUDY IN NORWAY, 1996-2001

Boyles AL, DeRoo LA, Lie RT, Taylor JA, Jugessur A, Murray JC, Wilcox AJ.
Epidemiology Branch, National Institute of Environmental Health Sciences, Durham, North Carolina 27709, USA. boylesa@niehs.nih.gov

ABSTRACT
Heavy maternal alcohol consumption during early pregnancy increases the risk of oral clefts, but little is known about how genetic variation in alcohol metabolism affects this association. Variants in the alcohol dehydrogenase 1C (ADH1C) gene may modify the association between alcohol and clefts. In a population-based case-control study carried out in Norway (1996-2001), the authors examined the association between maternal alcohol consumption and risk of oral clefts according to mother and infant ADH1C haplotypes encoding fast or slow alcohol-metabolizing phenotypes. Subjects were 483 infants with oral cleft malformations and 503 control infants and their mothers, randomly selected from all other livebirths taking place during the same period. Mothers who consumed 5 or more alcoholic drinks per sitting during the first trimester of pregnancy had an elevated risk of oral cleft in their offspring (odds ratio (OR) = 2.6, 95% confidence interval (CI): 1.4, 4.7). This increased risk was evident only in mothers or children who carried the ADH1C haplotype associated with reduced alcohol metabolism (OR= 3.0, 95% CI: 1.4, 6.8). There was no evidence of alcohol-related risk when both mother and infant carried only the rapid-metabolism ADH1C variant (OR = 0.9, 95% CI: 0.2, 4.1). The teratogenic effect of alcohol may depend on the genetic capacity of the mother and fetus to metabolize alcohol.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20810466

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PubMed, Int J Public Health. 2010 Sep 1. [Epub ahead of print]

24) KNOWLEDGE, ATTITUDES, AND BEHAVIORS OF HEALTH, EDUCATION, AND SERVICE PROFESSIONALS AS RELATED TO FETAL ALCOHOL SPECTRUM DISORDERS

Johnson ME, Robinson RV, Corey S, Dewane SL, Brems C, Diane Casto L.
Center for Behavioral Health Research and Services, University of Alaska Anchorage, Anchorage, AK, USA, afmej@uaa.alaska.edu.

ABSTRACT

Objectives: We explored differences in fetal alcohol spectrum disorders (FASD) knowledge, attitudes, and behaviors across six groups of professionals in key position to provide primary and secondary prevention efforts (physicians, educators, correctional staff, social workers, public health nurses, and substance abuse counselors).

Methods: Achieving a 60.1% response rate, 2,292 professionals returned surveys, providing data on basic knowledge of FAS, FASD-associated risks and cognitive deficits, and willingness to confront and recommend treatment to alcohol-consuming pregnant women.

Results: Across groups, findings revealed ample FASD knowledge and willingness to confront and recommend treatment to alcohol-consuming pregnant women that increases as consumption becomes more frequent and severe. However, results revealed significant between-group differences data that provide valuable guidance for targeted future FASD education efforts.

Conclusions: Public health initiatives regarding FASD have been effective in increasing knowledge among a broad range of professionals. However, between-group differences indicate the need for targeted, discipline-specific interventions. These differences highlight the need for all professional groups to provide a consistent public health message regarding maternal alcohol consumption.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20809348

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Wiley, British Journal of Special Education. Volume 37, Issue 3, pages 122–129, September 2010

25) FOETAL ALCOHOL SPECTRUM DISORDERS (FASD): RAISING AWARENESS IN EARLY YEARS SETTINGS (TRAINING AND DEVELOPMENT AGENCY – UK)

Carolyn Blackburn, Teresa Whitehurst

ABSTRACT

In this article Carolyn Blackburn who is currently project officer for the Training and Development Agency for Schools and Teresa Whitehurst who is a research and development officer at Sunfield School in Worcestershire discuss how educationalists are being required to support an increasing number of children with new and emerging disabilities including Foetal Alcohol Spectrum Disorders (FASD) for which they may be ill equipped if knowledge and resources are not available. FASD is an umbrella term used to describe a range of intellectual and physical disabilities that may occur when alcohol is consumed by the mother during pregnancy. This may lead to learning difficulties in the areas of gross and fine motor control, social and emotional development, hyperactivity and attention disorders, understanding rules and cause and effect, receptive and expressive language, and problem solving and numeracy. Educating and caring for these children needs a unique approach that relies on reflective practice and adaptive teaching techniques. This article focuses on a collaborative project

with Worcestershire Early Years entitled Building Bridges with Understanding. The project focused on raising awareness and increasing knowledge of FASD in early years practitioners to support children with a range of difficulties and provides access to a free downloadable resource pack.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1111/j.1467-8578.2010.00471.x/full

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PubMed, Glia. 2010 Sep;58(12):1395-406.

26) ETHANOL INHIBITS NEURITOGENESIS INDUCED BY ASTROCYTE MUSCARINIC RECEPTORS

Guizzetti M, Moore NH, Giordano G, VanDeMark KL, Costa LG.
Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA 98105, USA. marinag@u.washington.edu

ABSTRACT
In utero alcohol exposure can lead to fetal alcohol spectrum disorders, characterized by cognitive and behavioral deficits. In vivo and in vitro studies have shown that ethanol alters neuronal development. We have recently shown that stimulation of M(3) muscarinic receptors in astrocytes increases the synthesis and release of fibronectin, laminin, and plasminogen activator inhibitor-1, causing neurite outgrowth in hippocampal neurons. As M(3) muscarinic receptor signaling in astroglial cells is strongly inhibited by ethanol, we hypothesized that ethanol may also inhibit neuritogenesis in hippocampal neurons induced by carbachol-stimulated astrocytes. In the present study, we report that the effect of carbachol-stimulated astrocytes on hippocampal neuron neurite outgrowth was inhibited in a concentration-dependent manner (25-100 mM) by ethanol. This effect was because of the inhibition of the release of fibronectin, laminin, and plasminogen activator inhibitor-1. Similar effects on neuritogenesis and on the release of astrocyte extracellular proteins were observed after the incubation of astrocytes with carbachol in the presence of 1-butanol, another short-chain alcohol, which like ethanol is a competitive substrate for phospholipase D, but not by tert-butanol, its analog that is not a substrate for this enzyme. This study identifies a potential novel mechanism involved in the developmental effects of ethanol mediated by the interaction of ethanol with cell signaling in astrocytes, leading to an impairment in neuron-astrocyte communication.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20648635

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Oxford Journals, Alcohol and Alcoholism (2010). Accepted: 27th August 2010

27) CEREBRAL PALSY AND ALCOHOL CONSUMPTION DURING PREGNANCY: IS THERE A CONNECTION?

Ernest L. Abel.
Department of Obstetrics, C.S. Mott Center for Human Growth and Development, Wayne State University, 275 East Hancock, Detroit, MI 48201, USA
Department of Gynecology and Psychology, C.S. Mott Center for Human Growth and Development, Wayne State University, 275 East Hancock, Detroit, MI 48201, USA

ABSTRACT
Fetal alcohol syndrome (FAS) is a clinically identifiable diagnosis, consisting of pre- and/or postnatal growth retardation (below the third percentile), characteristic facial features, including a thin upper lip,

indistinct philtrum and short palpebral fissures (two standard deviations below normal for age), and neurobehavioral abnormalities (Abel, 1998; Jones et al., 1973; Plant, 1987; Sokol et al., 2003). Although FAS is the leading known cause of mental retardation in the USA (Abel and Sokol, 1986), brain injury involving milder forms of cognitive dysfunction, and more subtle and complex patterns of neurological impairment, occur in ~30–40% of children born to heavy drinkers, with or without the classic diagnostic features of FAS (Koren et al., 2003; Mattson et al., 1997). These neurodevelopmental disorders and other wide-ranging physical and behavioral problems occurring in conjunction with or in the absence of classic FAS features, are now subsumed under the broader umbrella term, fetal alcohol spectrum disorder (FASD). Many of these alcohol-related neurological impairments, e.g. hypotonia, clumsiness, unsteady gait, fine motor impairment, poor eye-hand coordination (Abel, 1998; Aronson et al., 1985; Barr et al., 1990; Jones et al., 1973; Marcus, 1987), stiff muscles and muscle spasms characterized as 'spasticity' (Beattie et al., 1983) are also hallmarks of cerebral palsy(CP; Lin, 2003). Despite these commonalities, the American College of Obstetricians and Gynecologists (ACOG) and …

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http://alcalc.oxfordjournals.org/content/early/2010/09/29/alcalc.agq063.extract?sid=6eaaf3f4-c87a-423b-b0d3-1165a1e0bfd9

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PubMed, BMC Public Health. 2010 Aug 23;10:510.

28) WOMEN'S KNOWLEDGE AND ATTITUDES REGARDING ALCOHOL CONSUMPTION IN PREGNANCY: A NATIONAL SURVEY

Peadon E, Payne J, Henley N, D'Antoine H, Bartu A, O'Leary C, Bower C, Elliott EJ.
Discipline of Paediatrics and Child Health, Sydney Medical School, The University of Sydney, The Children's Hospital at Westmead, Locked Bag 4001, Westmead, NSW 2145, Australia. elizabp5@chw.edu.au

ABSTRACT

Background: Alcohol exposure in pregnancy is a common and modifiable risk factor for poor pregnancy and child outcomes. Alcohol exposure in pregnancy can cause a range of physical and neurodevelopmental problems in the child including the Fetal Alcohol Spectrum Disorders (FASD). In order to improve prevention strategies, we sought to describe the knowledge and attitudes of women of childbearing age regarding alcohol consumption during pregnancy and its effects on the fetus.

Methods: We conducted a national cross-sectional survey via computer assisted telephone interview of 1103 Australian women aged 18 to 45 years. Participants were randomly selected from the Electronic White Pages. Pregnant women were not eligible to participate. Quotas were set for age groups and a minimum of 100 participants per state to ensure a national sample reflecting the population. The questionnaire was based on a Health Canada survey with additional questions constructed by the investigators. Descriptive statistics were calculated and logistic regression analyses were used to assess associations with participants' knowledge and attitudes.

Results: Of women surveyed, 61.5% had heard about effects of alcohol on the fetus and 55.3% had heard of Fetal Alcohol Syndrome. Although 92.7% agreed alcohol can affect the unborn child, 16.2% did not agree that the disabilities could be lifelong. Most women agreed that pregnant women should not drink alcohol (80.2%) and 79.2% reported having negative feelings towards pregnant women drinking alcohol. Women with higher education levels were more likely to know the effects of alcohol consumption in pregnancy (adjusted OR 5.62; 95% CI 3.20 to 9.87) but education level and knowledge were not associated with attitude.

Conclusions: There was a disjunction between knowledge and attitudes towards alcohol consumption in pregnancy. These findings will assist in developing effective health promotion campaigns to reduce fetal alcohol exposure and subsequent fetal damage.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20727217

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PubMed, Horm Behav. 2010 Aug 22. [Epub ahead of print]

29) PRENATAL ALCOHOL EXPOSURE REDUCES THE PROPORTION OF NEWLY PRODUCED NEURONS AND GLIA IN THE DENTATE GYRUS OF THE HIPPOCAMPUS IN FEMALE RATS

Uban KA, Sliwowska JH, Lieblich S, Ellis LA, Yu WK, Weinberg J, Galea LA.
Department of Psychology, The University of British Columbia, Vancouver, British Columbia, Canada.

ABSTRACT
Prenatal alcohol exposure (PAE) alters adult neurogenesis and the neurogenic response to stress in male rats. As the effects of stress on neurogenesis are sexually dimorphic, the present study investigated the effects of PAE on adult hippocampal neurogenesis under both nonstressed and stressed conditions in female rats. Pregnant females were assigned to one of three prenatal treatments: (1) alcohol (PAE)-liquid alcohol (ethanol) diet ad libitum (36% ethanol-derived calories); (2) pair-fed-isocaloric liquid diet, with maltose-dextrin substituted for ethanol, in the amount consumed by a PAE partner (g/kg body wt/day of gestation); and (3) control-lab chow ad libitum. Female offspring were assigned to either nonstressed (undisturbed) or stressed (repeated restraint stress for 9days) conditions. On day 10, all rats were injected with bromodeoxyuridine (BrdU) and perfused either 24hours (cell proliferation) or 3weeks (cell survival) later. We found that PAE did not significantly alter cell proliferation or survival, whereas females from the pair-fed condition exhibited elevated levels of cell survival compared to control females. Importantly, however, the proportion of both new neurons and new glial cells in the hippocampal dentate gyrus was reduced in PAE compared to control females. Exposure to stress did not alter neurogenesis in any of the prenatal treatment groups. In summary, compared to females from the control condition, prenatal dietary restriction enhanced the survival of new neurons, whereas PAE altered the differentiation of newly produced cells in the adult dentate gyrus. Alterations in hippocampal neurogenesis following PAE may contribute to learning and memory deficits seen in individuals with fetal alcohol spectrum disorders.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20736015

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J Popul Ther Clin Pharmacol Vol 17(2) Summer 2010:e308-e322; August 20, 2010

30) A LONG JOURNEY: BIOLOGICAL AND NON-BIOLOGICAL PARENTS' EXPERIENCES RAISING CHILDREN WITH FASD

James L Sanders, George Buck

ABSTRACT
Background: Research evaluating the experiences of birth and adoptive parents raising children with a fetal alcohol spectrum disorder (FASD) is needed to ascertain facilitating factors and barriers to

successful family functioning. Qualitative approaches to parents' experiences can help us better understand in what ways families need support and can also be used to guide quantitative research in this area.

Objectives: The present study is a qualitative, descriptive investigation of parents' experiences raising children with FASD in an Alberta city and environs.

Methods: Eleven participants, consisting of biological (3), adoptive (7), and foster (1) parents were interviewed using an unstructured format in order to enable them to share their "as-is" experience. A phenomenological-hermeneutic approach and thematic analysis was used to analyze and organize the data into themes.

Results: Nine central themes were derived from the interviews: 1) something's not right; 2) receiving a diagnosis; 3) attitudes toward birth parents; 4) living in a war zone; 5) understanding my child; 6) getting support; 7) re-defining success; 8) lifelong parenting; and 9) my child's gifts. Sub-themes were derived from several of these central themes. Descriptions of central and sub-themes are provided as data from each are presented.

Conclusions: By better understanding parents' experiences, family members, teachers, professionals, support personnel, and the community can better support parents of children with FASD. This support is needed in order to promote stable environments for families raising children with FASD, which has been identified as a critical protective factor to promote lifelong successes for those living with the disorder.

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http://www.cjcp.ca/pubmed.php?articleId=275

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PubMed, Behav Brain Res. 2010 Aug 20. [Epub ahead of print]

31) ACUTE PRENATAL EXPOSURE TO ETHANOL AND SOCIAL BEHAVIOR: EFFECTS OF AGE, SEX, AND TIMING OF EXPOSURE

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ABSTRACT

During development of the central nervous system, neurons pass through critical periods of vulnerability to environmental factors. Exposure to ethanol during gastrulation or during neuronal generation results in a permanent reduction in the number of neurons in trigeminal-associated cranial nerve nuclei. Normal functioning of the trigeminal system is required for social behavior, the present study examined the effects of acute prenatal exposure to ethanol on social interactions across ontogeny. Pregnant Long-Evans rats were injected with 2.9g/kg ethanol (i.p., 20%, v/v solution; peak blood ethanol concentrations of ~300mg/dl) or an equivalent volume of saline on gestational day (G) 7 (gastrulation) or G12 (neuronal generation). Subsequently, social investigation, play fighting, contact behavior, social motivation, and overall locomotor activity in the social context were assessed in male and female off-spring during early adolescence, late adolescence, or adulthood, on postnatal day (P) 28, P42, or P75, respectively, using a modified social interaction test. Ethanol exposure on G7 resulted in mild changes of social behavior evident in young adolescents only. In contrast, animals exposed to ethanol on G12 demonstrated pronounced behavioral deficits throughout ontogeny, with

deficits being most robust in male off-spring. Males exposed to ethanol on G12 showed decreases in social investigation, contact behavior, and play fighting, whereas a decrease in social motivation, i.e., transformation of social preference into social avoidance, was evident at P42 and P75 regardless of sex. These findings show that acute exposure to ethanol alters social behavior, and that the timing of the exposure defines the behavioral outcome.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20728475

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PubMed, Psychopharmacology (Berl). 2010 Aug 18. [Epub ahead of print]

32) PRENATAL ALCOHOL EXPOSURE AND CORTISOL ACTIVITY IN 19-MONTH-OLD TODDLERS: AN INVESTIGATION OF THE MODERATING EFFECTS OF SEX AND TESTOSTERONE

Ouellet-Morin I, Dionne G, Lupien SJ, Muckle G, Côté S, Pérusse D, Tremblay RE, Boivin M. MRC Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, De Crespigny Park, London, SE5 8AF, UK.

ABSTRACT

Rationale: Early exposure to stress and teratogenic substances have an impact on brain structures involved in cognition and mental health. While moderate-to-high levels of prenatal alcohol exposure (PAE) have repeatedly been associated with long-term neurodevelopmental deficits, no consensus has yet been reached on the detrimental effects of low-to-moderate PAE on the children's functioning, including the limbic-hypothalamic-pituitary-adrenal axis.

Objectives: The study aims to examine the association between low PAE and cortisol response to unfamiliar situations in 19-month-old children and to determine whether this association was moderated by sex and testosterone levels.

Methods: Information regarding PAE, cortisol response to unfamiliar situations, and testosterone activity was available in a total of 130 children participating to the Québec Newborn Twin Study (Montréal, QC, Canada). Mother alcohol consumption during pregnancy was assessed via a semistructured interview conducted when the children were 6 months of age. The contribution of prenatal and postnatal confounds were examined.

Results: Disrupted patterns of cortisol activity were observed only in PAE males. Testosterone tended to be negatively associated with the cortisol response, but not for PAE males, suggesting an altered sensitivity to the inhibitory effects of testosterone in these participants.

Conclusions: Low levels of PAE were associated with disrupted cortisol activity, and males may be at higher risk. These findings challenge the existence of a "safe level" of alcohol consumption during pregnancy and have public health implications.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20717651

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J Popul Ther Clin Pharmacol Vol 17 (2) Summer 2010: e302-e307; August 17, 2010

33) DRINKING ALCOHOL DURING PREGNANCY: EVIDENCE FROM CANADIAN COMMUNITY HEALTH SURVEY 2007/ 2008

NX Thanh, E Jonsson

ABSTRACT

Background: Drinking alcohol during pregnancy may cause many health problems for the child, one of which is fetal alcohol spectrum disorder (FASD). Since FASD is incurable, actions meant to prevent the occurrence of the disability by targeting drinking women become more important. Epidemiological data on drinking among pregnant women, including prevalence and determinants/risk factors, is essential for designing and evaluating prevention programs.

Objectives: To estimate the prevalence of drinking alcohol during pregnancy and examine the determinants of this behaviour.

Methods: Using the 2007/8 Canadian Community Health Survey (CCHS) data, we estimated the weighted prevalence of women who drank alcohol during their last pregnancy by provinces. We used a weighted logistic regression to examine associations between drinking patterns, substance abuse behaviours, health-related and socio-demographic characteristics of the women, and the outcome variable.

Results: There were two main findings of this study. One was that the 2007/8 prevalence of drinking alcohol during pregnancy in ON, BC, and Canada was estimated at 5.4%, 7.2%, and 5.8%, respectively. The other was that the use of general practitioners (GP) or family physicians (FP) associated with a decreased risk of drinking alcohol during pregnancy.

Discussion:

The results suggest that interventions that involve GP or FP and that increase the use of GP or FP by pregnant women can be effective in reducing drinking alcohol during pregnancy.

Read Full Article,

http://www.cjcp.ca/pubmed.php?articleId=274

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PubMed, Arch Pediatr. 2010 Sep;17(9):1273-80. Epub 2010 Aug 16.

34) CONSEQUENCES FOR THE NEWBORN OF ALCOHOL CONSUMPTION DURING PREGNANCY

Toutain S, Simmat-Durand L, Crenn-Hébert C, Simonpoli AM, Vellut N, Genest L, Miossec E, Lejeune C.

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ABSTRACT

Background: This paper aims at showing the immediate and long-term consequences affecting newborns whose mothers did not reduce or stop their consumption of alcohol when they were pregnant; these women were chosen among women who also used psychoactive substances.

Methods: A retrospective cohort was constituted of babies who were found to have been exposed in utero to one or more legal or illegal psychoactive substance(s) and who were born or hospitalized

between 1999 and 2008 in a hospital near Paris. Among the cohort of 170 babies, 56 had mothers who had not modified their alcohol consumption when they were pregnant, 30 had mothers who had reduced their alcohol consumption, and 84 had mothers who declared having been abstinent.

Results: The babies born to mothers who did not modify their alcohol consumption when pregnant were more likely to be premature (30%) and hospitalized in the neonatology hospital unit (60.7%). They needed specific care for durations significantly longer than the babies exposed in utero to other psychoactive substances (P<0.005). They were more often diagnosed with fetal alcohol spectrum disorders (18%) and placed in a foster family (18%).

Conclusion: Given the negative consequences on the babies born to mothers who do not modify their alcohol consumption when pregnant, these mothers should be identified and provided with better care. The successful strategies for early therapeutic interventions used in other countries should be studied as examples. This would make it possible to reduce the enormous financial, material and human costs that are a direct consequence of alcohol consumption during pregnancy.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20719484

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PubMed, Birth Defects Res A Clin Mol Teratol. 2010 Aug 12. [Epub ahead of print]

35) PRENATAL CHOLINE SUPPLEMENTATION MITIGATES BEHAVIORAL ALTERATIONS ASSOCIATED WITH PRENATAL ALCOHOL EXPOSURE IN RATS

Thomas JD, Idrus NM, Monk BR, Dominguez HD.
Center for Behavioral Teratology, Department of Psychology, San Diego State University, San Diego, California.

ABSTRACT
Background: Prenatal alcohol exposure can alter physical and behavioral development, leading to a range of fetal alcohol spectrum disorders. Despite warning labels, pregnant women continue to drink alcohol, creating a need to identify effective interventions to reduce the severity of alcohol's teratogenic effects. Choline is an essential nutrient that influences brain and behavioral development. Recent studies indicate that choline supplementation can reduce the teratogenic effects of developmental alcohol exposure. The present study examined whether choline supplementation during prenatal ethanol treatment could mitigate the adverse effects of ethanol on behavioral development.

Methods: Pregnant Sprague-Dawley rats were intubated with 6 g/kg/day ethanol in a binge-like manner from gestational days 5-20; pair-fed and ad libitum chow controls were included. During treatment, subjects from each group were intubated with either 250 mg/kg/day choline chloride or vehicle. Spontaneous alternation, parallel bar motor coordination, Morris water maze, and spatial working memory were assessed in male and female offspring.

Results: Subjects prenatally exposed to alcohol exhibited delayed development of spontaneous alternation behavior and deficits on the working memory version of the Morris water maze during adulthood, effects that were mitigated with prenatal choline supplementation. Neither alcohol nor choline influenced performance on the motor coordination task.

Conclusions: These data indicate that choline supplementation during prenatal alcohol exposure may reduce the severity of fetal alcohol effects, particularly on alterations in tasks that require behavioral

flexibility. These findings have important implications for children of women who drink alcohol during pregnancy. Birth Defects Research (Part A), 2010

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20706995

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PubMed, J Speech Lang Hear Res. 2010 Aug 12. [Epub ahead of print]

36) OBSERVATION OF CLASSROOM SOCIAL COMMUNICATION: DO CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS SPEND THEIR TIME DIFFERENTLY THAN THEIR PEERS DEVELOPING TYPICALLY?

Olswang LB, Svensson L, Astley S.
Professor, Department of Speech and Hearing Sciences, University of Washington, Seattle, WA.

ABSTRACT
Purpose: This research examined how social communication profiles during classroom activities differed between children with fetal alcohol spectrum disorders (FASD) and pair-matched peers developing typically.

Methods: Twelve pairs of children were observed in their classrooms, 20 minutes a day for four days across two weeks. Coders documented classroom social communication by recording performance on handheld computers using the Social Communication Coding System (SCCS). The SCCS consists of six behavioral dimensions (prosocial/engaged, passive/disengaged, irrelevant, hostile/coercive, assertive, and adult seeking) that account for all verbal and nonverbal productions during a specified time frame. The frequency of occurrence and duration of each dimension (as measured by proportion of time and average length of time spent performing each dimension) was recorded.

Results: Children with FASD had significantly more occurrences of passive/disengaged and irrelevant behavior, and the proportion and average length of time in these behaviors were larger and longer than their peers'. Further, they had significantly more occurrences of prosocial/engaged behavior; however, the proportion and average length of time they spent being prosocial were smaller and shorter than their peers'.

Implications: Results suggest children with mild FASD performed differently than their peers in regard to classroom social communication, consistent with parent and teacher behavioral reports.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20705742

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PubMed, Alcohol. 2010 Aug 11. [Epub ahead of print]

37) SUBTLE DECREASES IN DNA METHYLATION AND GENE EXPRESSION AT THE MOUSE IGF2 LOCUS FOLLOWING PRENATAL ALCOHOL EXPOSURE: EFFECTS OF A METHYL-SUPPLEMENTED DIET

Downing C, Johnson TE, Larson C, Leakey TI, Siegfried RN, Rafferty TM, Cooney CA.
Institute for Behavioral Genetics, University of Colorado, Boulder, CO 80309-0447, USA.

ABSTRACT
C57BL/6J (B6) mice are susceptible to in utero growth retardation and a number of morphological malformations following prenatal alcohol exposure, while DBA/2J (D2) mice are relatively resistant.

We have previously shown that genomic imprinting may play a role in differential sensitivity between B6 and D2. The best-characterized mechanism mediating genomic imprinting is differential DNA methylation. In the present study we examined DNA methylation and gene expression, in both embryonic and placental tissue, at the mouse Igf2 locus following in utero ethanol exposure. We also examined the effects of a methyl-supplemented diet on methylation and ethanol teratogenesis. In embryos from susceptible B6 mice, we found small decreases in DNA methylation at four CpG sites in one of the differentially methylated regions of the Igf2 locus; only one of the four sites showed a statistically significant decrease. We observed no significant decreases in methylation in placentae. All Igf2 transcripts showed approximately 1.5-fold decreases following intrauterine alcohol exposure. Placing dams on a methyl-supplemented diet before pregnancy and throughout gestation brought methylation back up to control levels. Methyl supplementation also resulted in lower prenatal mortality, greater prenatal growth, and decreased digit malformations; it dramatically reduced vertebral malformations. Thus, although prenatal alcohol had only small effects on DNA methylation at the Igf2 locus, placing dams on a methyl-supplemented diet partially ameliorated ethanol teratogenesis.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20705422

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PubMed, Alcohol. 2010 Aug 11. [Epub ahead of print]

38) ETHANOL EXPOSURE DURING THE EARLY FIRST TRIMESTER EQUIVALENT IMPAIRS REFLEXIVE MOTOR ACTIVITY AND HEIGHTENS FEARFULNESS IN AN AVIAN MODEL

Department of Nutritional Sciences, University of Wisconsin-Madison, Madison WI 53706, USA; Waisman Center for Neurodevelopmental Disabilities, University of Wisconsin-Madison, Madison WI 53706, USA.

ABSTRACT
Prenatal alcohol exposure is a leading cause of childhood neurodevelopmental disability. The adverse behavioral effects of alcohol exposure during the second and third trimester are well documented; less clear is whether early first trimester-equivalent exposures also alter behavior. We investigated this question using an established chick model of alcohol exposure. In ovo embryos experienced a single, acute ethanol exposure that spanned gastrulation through neuroectoderm induction and early brain patterning (19-22h incubation). At 7 days posthatch, the chicks were evaluated for reflexive motor function (wingflap extension, righting reflex), fearfulness (tonic immobility [TI]), and fear/social reinstatement (open-field behavior). Chicks exposed to a peak ethanol level of 0.23-0.28% were compared against untreated and saline-treated controls. Birds receiving early ethanol exposure had a normal righting reflex and a significantly reduced wingflap extension in response to a sudden descent. The ethanol-treated chicks also displayed heightened fearfulness, reflected in increased frequency of TI, and they required significantly fewer trials for its induction. In an open-field test, ethanol treatment did not affect latency to move, steps taken, vocalizations, defecations, or escape attempts. The current findings demonstrate that early ethanol exposure can increase fearfulness and impair aspects of motor function. Importantly, the observed dysfunctions resulted from an acute ethanol exposure during the period when the major brain components are induced and patterned. The equivalent period in human development is 3-4 weeks postconception. The current findings emphasize that ethanol exposure during the early first trimester equivalent can produce neurodevelopmental disability in the offspring.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20705421

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PubMed, Alcohol. 2010 Aug 11. [Epub ahead of print]

39) AN IMPROVED METHOD FOR RAPIDLY QUANTIFYING FATTY ACID ETHYL ESTERS IN MECONIUM SUITABLE FOR PRENATAL ALCOHOL SCREENING

Hutson JR, Rao C, Fulga N, Aleksa K, Koren G.
Motherisk Laboratory, Hospital for Sick Children, Toronto, Ontario M5G 1X8, Canada; Institute of Medical Science, University of Toronto, Toronto, Ontario M5S 1A8, Canada.

ABSTRACT
Fatty acid ethyl esters (FAEEs) are nonoxidative metabolites of ethanol, and elevated levels of FAEE in meconium are a useful biomarker for heavy prenatal alcohol exposure. FAEE in meconium has been recommended as useful and cost-effective for universal screening for prenatal alcohol exposure. To support an efficient universal screening program, an analytical method to detect and quantify FAEE in meconium needs to be accurate, inexpensive, and rapid. The purpose of this study was to develop an analytical method that would satisfy these criteria and to validate this method using established laboratory guidelines. A method was developed and validated to detect and quantify four FAEEs (ethyl palmitate, ethyl linoleate, ethyl oleate, and ethyl stearate) from 0.5g of meconium using d(5)-ethyl esters as internal standards. The sample undergoes liquid-liquid extraction with heptane:acetone, the heptane layer is isolated and evaporated, and then, the resulting residue undergoes headspace solid-phase microextraction coupled with gas chromatography-mass spectrometry. The detection limits of the four FAEEs ranged from 0.020 to 0.042nmol/g and are 6- to 25-fold lower than the individual FAEE threshold concentrations (0.5nmol/g). This method also has good precision with the coefficient of variation ranging from 2.6 to 19.4% for concentrations of individual FAEE between 0.5 and 2.62nmol/g meconium (n=4). Calculated concentrations of FAEE that underwent extraction from meconium were 100-101% of the expected concentration, demonstrating the accuracy of the method. The peak shape and retention time of each FAEE were unaffected by the presence of the matrix, and there is no carryover at clinically relevant concentrations. This method was also able to produce clean chromatograms from meconium samples that could not be quantified using a previous method because of high chromatographic background. This method provides an optimal approach to detecting and quantifying FAEE in meconium that could be used in a universal screening program for prenatal alcohol exposure.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20705417

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PubMed, Community Ment Health J. 2010 Aug 8. [Epub ahead of print]

40) THE EFFECTIVENESS OF A COMMUNITY-BASED INTERVENTION PROGRAM FOR WOMEN AT-RISK FOR GIVING BIRTH TO A CHILD WITH FETAL ALCOHOL SPECTRUM DISORDER (FASD)

Rasmussen C, Kully-Martens K, Denys K, Badry D, Henneveld D, Wyper K, Grant T.
University of Alberta, 266, Glenrose Rehabilitation Hospital, 10230-111 Ave, Edmonton, AB, T5G 0B7, Canada, carmen@ualberta.ca.

ABSTRACT
The goal of this study was to determine whether the First Steps program (modeled after the Parent-Child Assistance Program) resulted in improved outcomes among women at-risk for giving birth to a child with FASD. We conducted a retrospective analysis of data on 70 participants in the First Steps program. Clients were high risk and faced many life challenges, including: being on welfare, substance

abuse, physical and sexual abuse as children, mental health issues, criminal activity, and unplanned pregnancies. We found a significant increase in birth control use and decrease in welfare rates from pre- to post-program. At program exit, many participants were abstinent from alcohol and/or drugs and the majority did not experience a subsequent pregnancy. Clients also showed significant increases in goals and decreases in needs from pre-to post-program. The First Steps program demonstrated promising outcomes for women at-risk for giving birth to a child with FASD.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20694802

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PubMed, Neuroscience. 2010 Nov 10;170(4):1328-44. Epub 2010 Aug 5.

41) INHIBITION OF CEREBELLAR GRANULE CELL TURNING BY ALCOHOL

Kumada T, Komuro Y, Li Y, Hu T, Wang Z, Littner Y, Komuro H.
Department of Neurosciences, Lerner Research Institute, The Cleveland Clinic Foundation, Cleveland, OH 44195, USA.

ABSTRACT
Ectopic neurons are often found in the brains of fetal alcohol spectrum disorders (FASD) and fetal alcohol syndrome (FAS) patients, suggesting that alcohol exposure impairs neuronal cell migration. Although it has been reported that alcohol decreases the speed of neuronal cell migration, little is known about whether alcohol also affects the turning of neurons. Here we show that ethanol exposure inhibits the turning of cerebellar granule cells in vivo and in vitro. First, in vivo studies using P10 mice demonstrated that a single intraperitoneal injection of ethanol not only reduces the number of turning granule cells but also alters the mode of turning at the EGL-ML border of the cerebellum. Second, in vitro analysis using microexplant cultures of P0-P3 mouse cerebella revealed that ethanol directly reduces the frequency of spontaneous granule cell turning in a dose-dependent manner. Third, the action of ethanol on the frequency of granule cell turning was significantly ameliorated by stimulating Ca(2+) and cGMP signaling or by inhibiting cAMP signaling. Taken together, these results indicate that ethanol affects the frequency and mode of cerebellar granule cell turning through alteration of the Ca(2+) and cyclic nucleotide signaling pathways, suggesting that the abnormal allocation of neurons found in the brains of FASD and FSA patients results, at least in part, from impaired turning of immature neurons by alcohol.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20691765

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PubMed, Neuroscience. 2010 Oct 27;170(3):749-57. Epub 2010 Aug 3.

42) PRENATAL ETHANOL EXPOSURE ATTENUATES GABAERGIC INHIBITION IN BASOLATERAL AMYGDALA LEADING TO NEURONAL HYPEREXCITABILITY AND ANXIETY-LIKE BEHAVIOR OF ADULT RAT OFFSPRING

Zhou R, Wang S, Zhu X.
Department of Physiology, Nanjing Medical University, Hanzhong Road 140, Jiangsu, PR China. zhou-rong@hotmail.com

ABSTRACT
Prenatal exposure to a relatively high-dose ethanol (EtOH) caused anxiety-like behavior of adult male rat offspring. Previous studies have demonstrated that GABA system in the basolateral amygdala

complex (BLA) is involved in the pathogensis of anxiety-related disorders. The role of GABAergic system in the BLA was investigated in anxiety-like behavior evoked by prenatal EtOH exposure. The infusion of midazolam (MDZ), a positive modulator of GABA(A) receptor, into the BLA prevented anxiety-like behavior in EtOH-offspring without affecting the corresponding behavior of control offspring. The data suggest that anxiety-like behavior could be causally related to increased neuronal excitability attributable to depressed GABAergic inhibition in the BLA. To test this hypothesis, evoked potential was studied using brain slices from EtOH-offspring. Potential evoked in the BLA by single stimuli applied to external capsule showed multispike responses, indicative of GABAergic disinhibition. These multiple responses were no longer evident after the perfusion with MDZ. In the slices from EtOH-offspring, paired-pulse inhibition (GABA(A)-dependent) was suppressed. Also, in EtOH-offspring, long-term potentiation (LTP) was induced by a single train of high frequency stimulation, which did not induce LTP in control rats. Moreover, MDZ pretreatment prevented the facilitating effect of EtOH on LTP induction. The data provide the functional evidence that prenatal EtOH exposure attenuates GABAergic inhibition in the BLA resulting in neuronal hyperexcitability and anxiety-like behavior of adult rat offspring.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20688136

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PubMed, Pediatr Neurol. 2010 Aug;43(2):110-6.

43) FETAL ALCOHOL SYNDROME, TOURETTE SYNDROME, AND HYPERACTIVITY IN NINE ADOPTED CHILDREN

Fernández-Mayoralas DM, Fernández-Jaén A, Muñoz-Jareño N, Calleja Pérez B, Arroyo-González R. Department of Neuropediatrics, Hospital Quirón, Pozuelo de Alarcón (Madrid), Spain. dmfmayor@yahoo.es

ABSTRACT
Much attention has been paid in recent years to the role of prenatal exposure to alcohol. Fetal alcohol syndrome is one of the most severe afflictions resulting from such exposure. The present report documents the cases of adopted children diagnosed with fetal alcohol syndrome who developed both Tourette syndrome and attention deficit-hyperactivity disorder. Out of a population of 138 adopted children with behavior issues whose clinical histories were reviewed retrospectively, 9 children (6.5%) presented this constellation. Epidemiologic data, clinical data, neurologic examination findings, complementary testing, and developmental data were recorded. All nine patients studied had initial psychomotor retardation, despite the frequent case of subsequent intelligence quotient normalization. From a behavioral perspective, half of the cases presented obsessive-compulsive disorder and problems with social relations. Aggressive behavior was common. These cases also presented a high degree of severity of both tics and hyperactivity. The most common drug treatment was methylphenidate. This constellation of fetal alcohol syndrome, Tourette syndrome, and attention deficit-hyperactivity disorder is scantly reported in the literature and is likely underdiagnosed. This particular constellation poses its own prognosis and requires its own treatment.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20610121

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PubMed, Subst Use Misuse. 2010 Aug;45(10):1474-90.

44) HEALTH PROFESSIONALS ADDRESSING ALCOHOL USE WITH PREGNANT WOMEN IN WESTERN AUSTRALIA: BARRIERS AND STRATEGIES FOR COMMUNICATION

France K, Henley N, Payne J, D'Antoine H, Bartu A, O'Leary C, Elliott E, Bower C.
Centre for Child Health Research, Telethon Institute for Child Health Research, The University of Western Australia, West Perth, WA, Australia. kathrynf@ichr.uwa.edu.au

ABSTRACT
Health professionals have an important role to play in preventing prenatal alcohol exposure. In 2006 qualitative data were collected from 53 health professionals working in primary care in metropolitan and regional Western Australia. Thematic analysis was used to elucidate barriers in addressing prenatal alcohol use and the strategies used to overcome them. Health professionals identified strategies for obtaining alcohol use information from pregnant women but they are not recognizing moderate alcohol intake in pregnant women. Study limitations are noted and the implications of the results are discussed. This research was funded by the Health Promotion Foundation of Western Australia.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20590371

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PubMed, Midwifery. 2010 Aug;26(4):430-4. Epub 2009 Jan 29.

45) APPROACHES TO ASSESSMENT OF ALCOHOL INTAKE DURING PREGNANCY IN SWEDISH MATERNITY CARE—A NATIONAL-BASED INVESTIGATION INTO MIDWIVES' ALCOHOL-RELATED EDUCATION, KNOWLEDGE AND PRACTICE

Holmqvist M, Nilsen P.
Department of Medical and Health Sciences, Division of Social Medicine and Public Health Science, Linköping University, SE-581 83 Linköping, Sweden. mahol@ihs.liu.se

ABSTRACT
Objective: to evaluate how much education midwives in Sweden have undertaken to help them assess alcohol intake during pregnancy, and what tools they use to identify women who may be at risk of drinking during pregnancy.

Design: a national survey was conducted in March 2006, using a questionnaire constructed by a Swedish team of researchers and clinicians.

Setting: Maternity health-care centres in Sweden.

Participant: 2106 midwives.

Findings: nearly all midwives stated that they had excellent or good knowledge concerning the risks associated with drinking during pregnancy. They considered themselves less knowledgeable about detecting pregnant women with risky alcohol consumption before pregnancy. The majority of the midwives had participated in some education in handling risky drinking. Almost half of the midwives assessed women's alcohol intake before pregnancy. Important facilitators for increased activity concerned recommendations and decisions at different levels (national, local and management) on how to address alcohol with expectant parents and work with risky drinkers.

Key Conclusions: more education was associated with more common use of a questionnaire for assessment of women's alcohol intake before pregnancy, and more frequent counselling when identifying a pregnant woman whose pre-pregnancy consumption was risky.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/19185397

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PubMed, Klin Padiatr. 2010 Jul 30. [Epub ahead of print]

46) YOUNG ADULTS WITH FETAL ALCOHOL SYNDROME (FAS): SOCIAL, EMOTIONAL AND OCCUPATIONAL DEVELOPMENT

Freunscht I, Feldmann R.
University Hospital, Pediatrics, Münster, Germany.

ABSTRACT
Background: Maternal alcohol abuse during pregnancy causes physical, cognitive and behavioural impairments in the child. Deficits are irreversible and persist into adulthood. It was the objective of this study to investigate the specific problems and challenges faced by young adults with Fetal Alcohol Syndrome (FAS).

Patients: We examined the biographical development and living situation of 60 adult patients with FAS. In their childhood, all the patients had been diagnosed with FAS in the Muenster University hospital.

Methods: Using a structured interview, we asked for the occupational career, health and social problems as well as the current living conditions of the patients.

Results: Most patients lived in dependent circumstances. The occupational development was characterized by disruption and failure, and severe social problems were common in patients. 3 in 4 patients were victims of physical and sexual abuse.

Conclusions: Due to the variety of impairments caused by prenatal alcohol exposure and the persisting inability to live independently, adults with FAS need intense care, support and assistance.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20677126

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PubMed, Exp Brain Res. 2010 Aug;205(2):263-71. Epub 2010 Jul 27.

47) REDUCED SOMA SIZE OF THE M-NEURONS IN THE LATERAL GENICULATE NUCLEUS FOLLOWING FOETAL ALCOHOL EXPOSURE IN NON-HUMAN PRIMATES

Papia MF, Burke MW, Zangenehpour S, Palmour RM, Ervin FR, Ptito M.
Ecole d'optométrie, Université de Montréal, Montréal, Canada.

ABSTRACT
Visual impairment is commonly reported as a consequence of heavy prenatal ethanol exposure in humans. Children generally display characteristic cranio-facial dysmorphology and represent typical

severe cases of foetal alcohol syndrome. Binge-like rodent model systems have concluded that third trimester equivalent ethanol exposure results in widespread apoptosis in the visual system from the retina to the visual cortex. Neither clinical nor animal studies address the consequences of more moderate prenatal ethanol exposure on the visual system. The current study uses a naturalistic and voluntary consumption approach in non-human primates (Chlorocebus sabeus) in order to more closely model prenatal ethanol consumption patterns in humans. Pregnant vervet monkeys voluntarily drank on average 2.418 +/- 0.296 g etoh/kg/day four times a week during the third trimester. Using unbiased stereology, we estimated the neuronal and glial population of the parvocellular (P) and magnocellular (M) layers of the lateral geniculate nucleus (LGN) following foetal alcohol exposure (FAE) in infant subjects. Layer volume and total number of neurons and glia in the LGN of the FAE subjects were not significantly different from age-matched control subjects. The M neuronal soma size of FAE subjects, however, was significantly reduced to resemble the size of the P-neurons. These results suggest that alterations at the level of morphology and anatomy of the M-neurons may lead to behavioural deficits associated with the integrity of the dorsal visual pathway.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20661554

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PubMed, Psychopharmacology (Berl). 2010 Jul 27. [Epub ahead of print]

48) FETAL ALCOHOL-INDUCED HYPERACTIVITY IS REVERSED BY TREATMENT WITH THE PPARALPHA AGONIST FENOFIBRATE IN A RAT MODEL

Marche K, Danel T, Bordet R.
EA1046 - Département de Pharmacologie Médicale - Centre Hospitalier Universitaire, Université Lille-Nord-de-France - Faculté de Médecine, 1, Place de Verdun, 59-045, Lille Cedex, France

ABSTRACT

Introduction: Exposure to alcohol in utero is linked to the development of a wide range of psychobehavioral changes, notably hyperactivity and attention deficit, with complex underlying pathological and functional mechanisms. Although the currently available treatments for hyperactivity have been studied in children exposed to alcohol in utero, the efficacy of these compounds is subject to debate and has prompted efforts to identify new pharmacological targets.

Method: In a rat model of early alcohol exposure (i.e., in utero and during lactation), we studied the effect of the lipid-lowering peroxisome proliferator-activated receptor (PPAR) alpha activator fenofibrate on psychobehavioral impairments.

Results: In the young rat, early exposure to alcohol perturbs locomotor behavior and induces prepubertal hyperactivity and postpubertal hypoactivity. The hyperactivity, usually observed at the end of the fifth week of life, was prevented by the administration of fenofibrate, which also had a beneficial effect on the accompanying attention deficit by reinforcing sustained attention.

Conclusion: Our results with fenofibrate suggest that the pharmacological modulation of nuclear receptors such as PPAR-alpha may constitute a new therapeutic approach to managing the psychobehavioral disorders associated with early alcohol exposure.

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http://www.ncbi.nlm.nih.gov/pubmed/20661551

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Wiley Online Library - Journal of Neurochemistry - Published Online: 27 July 2010

49) ETHANOL-INDUCED METHYLATION OF CELL CYCLE GENES IN NEURAL STEM CELLS
Steven D. Hicks, Frank A. Middleton, Michael W. Miller

ABSTRACT
Ethanol inhibits the proliferation of neural precursors by altering mitogenic and anti-mitogenic growth factor signaling and can affect global methylation activity in the fetus. We tested the hypothesis that epigenetic modification of specific cell cycle genes underlies the ethanol-induced inhibition of growth factor-regulated cell cycle progression. Monolayer cultures of neural stem cells (NSCs) were treated with fibroblast growth factor 2 or transforming growth factor (TGF) β1 in the absence or presence of ethanol. Ethanol increased the total length of the cell cycle by elongating the amount of time spent in the gap 1 (G1) and synthesis (S) phases of the cell cycle. Ethanol induced the hypermethylation of multiple cell cycle genes associated with the G1/S and gap 2/mitotic phase (G2/M) checkpoints and increased the expression and activity of DNA methyltransferases. These changes were most pronounced in the presence of TGFβ1. Epigenetic alterations paralleled the down-regulation of associated transcripts and other checkpoint-related mRNAs both in vitro (NS-5 cell culture) and in vivo (fetal mouse cortex). Ethanol-induced hypermethylation was accompanied by decreases in the proportion of NSCs expressing associated cell cycle proteins. Thus, ethanol disrupts growth factor-related cell cycle progression by inducing checkpoint restriction at the G1/S transition through a feed-forward system involving the methylation of G2/M regulators.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1111/j.1471-4159.2010.06886.x/abstract

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PubMed, Alcohol Clin Exp Res. 2010 Jul 23. [Epub ahead of print]

50) THE PREVENTIVE EFFECT OF ORAL EGCG IN A FETAL ALCOHOL SPECTRUM DISORDER MOUSE MODEL
Long L, Li Y, Wang YD, He QY, Li M, Cai XD, Peng K, Li XP, Xie D, Wen YL, Yin DL, Peng Y.
From the Departments of Neurology (LL, YL, YDW, ML, XDC, KP, XPL, YP) and Ultrasonography (YLW), The Second Affiliated Hospital, Sun Yat-Sen University, No. 107, West Yanjiang Road, Guangzhou, China; Institute of Life and Health Engineering (QYH), Jinan University, No. 601, West Huangpu Road, Guangzhou, China; State Key Laboratory of Oncology in South China (DX), Cancer Center, Sun Yat-Sen University, 651 Dongfeng East Road, Guangzhou, China; and Department of Internal Medicine (DLY), James Quillen College of Medicine, East Tennessee State University, Johnson City, Tennessee, U.S.A.

ABSTRACT
Background: Fetal alcohol spectrum disorder (FASD) is a challenging public health problem. Previous studies have found an association between FASD and oxidative stress. In the present study, we assessed the role of oxidative stress in ethanol-induced embryonic damage and the effect of (-)-epigallocatechin-3-gallate (EGCG), a powerful antioxidant extracted from green tea, on the development of FASD in a murine model.

Methods: Pregnant female mice were given intraperitoneal ethanol (25%, 0.005 to 0.02 ml/g) on gestational day 8 (G8) to establish the FASD model. On G10.25, mice were sacrificed and embryos were collected and photographed to determine head length (HL), head width (HW), and crown rump length (CRL). For mice given EGCG, administration was through a feeding tube on G7 and G8 (dose: 200, 300, or 400 mg/kg/d, the total amount for a day was divided into 2 equal portions). G10.25

embryos were evaluated morphologically. Brain tissues of G9.25 embryos were used for RT-PCR and western blotting of neural marker genes and proteins and detection of oxidative stress indicators.

Results: Administration of ethanol to pregnant mice on G8 led to the retardation of embryonic growth and down-regulation of neural marker genes. In addition, administration of ethanol (0.02 ml/g) led to the elevation of oxidative stress indicators [hydrogen peroxide (H(2)O(2)) and malondialdehyde (MDA)]. Administration of EGCG on G7 and G8 along with ethanol on G8 ameliorated the ethanol-induced growth retardation. Mice given EGCG (400 mg/kg/d) along with ethanol had embryo sizes and neural marker genes expression similar to the normal controls. Furthermore, EGCG (400 mg/kg on G7 and G8) inhibited the increase in H(2)O(2) and MDA.

Conclusions: In a murine model, oxidative stress appears to play an important role in ethanol-induced embryonic growth retardation. EGCG can prevent some of the embryonic injuries caused by ethanol.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20659071

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PubMed, Alcohol Clin Exp Res. 2010 Jul 21. [Epub ahead of print]

51) FETAL ALCOHOL EXPOSURE INCREASES MAMMARY TUMOR SUSCEPTIBILITY AND ALTERS TUMOR PHENOTYPE IN RATS

Polanco TA, Crismale-Gann C, Reuhl KR, Sarkar DK, Cohick WS.
From the Department of Animal Sciences (TAP, CCG, DKS, WSC), New Brunswick, and the Department of Pharmacology and Toxicology (KRR), Piscataway, Rutgers Endocrine Program, Rutgers, The State University of New Jersey.

ABSTRACT
Background: Altered fetal programming because of a suboptimal in utero environment has been shown to increase susceptibility to many diseases later in life. This study examined the effect of alcohol exposure in utero on N-nitroso-N-methylurea (NMU)-induced mammary cancer risk during adulthood.

Methods: Study 1: Pregnant Sprague Dawley rats were fed a liquid diet containing 6.7% ethanol (alcohol-fed), an isocaloric liquid diet (pair-fed), or rat chow ad libitum (ad lib-fed) from day 11 to 21 of gestation. At birth, female pups were cross-fostered to ad lib-fed control dams. Adult offspring were given an I.P. injection of NMU at a dose of 50 mg/kg body weight. Mammary glands were palpated for tumors twice a week, and rats were euthanized at 23 weeks postinjection. Study 2: To investigate the role of estradiol (E2), animals were exposed to the same in utero treatments but were not given NMU. Serum was collected during the preovulatory phase of the estrous cycle.

Results: At 16 weeks postinjection, overall tumor multiplicity was greater in the offspring from the alcohol-fed group compared to the control groups, indicating a decrease in tumor latency. At study termination, 70% of all animals possessed tumors. Alcohol-exposed animals developed more malignant tumors and more estrogen receptor-alpha-negative tumors relative to the control groups. In addition, IGF-binding protein-5 (IGFBP-5) mRNA and protein were decreased in tumors of alcohol-exposed animals. Study 2 showed that alcohol-fed animals had significantly increased circulating E2 when compared to either control group.

Conclusions: These data indicate that alcohol exposure in utero increases susceptibility to mammary tumorigenesis in adulthood and suggest that alterations in the IGF and E2 systems may play a role in the underlying mechanism.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20662802

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J Popul Ther Clin Pharmacol Vol 17 (2) Summer 2010: e281-e283; July 20, 2010

52) REVIEWERS' BIAS AGAINST THE NULL HYPOTHESIS: THE REPRODUCTIVE HAZARD OF BINGE DRINKING
Gideon Koren, Andrea Fernandes

ABSTRACT
We examined whether scientific reviewers exhibit bias in scoring a simulated “positive” study (i.e. showing adverse fetal effects) as compared to a simulated “negative” study on the fetal effects of binge drinking. The reviewers of the “negative” study tended to reject it more commonly, to give it lower scores, and there was significantly more variability from the median in their scores. Scientific journals should make an effort to eliminate this source of bias against negative results.

Read Full Article,
http://www.cjcp.ca/pubmed.php?articleId=270

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PubMed, Alcohol Clin Exp Res. 2010 Oct;34(10):1813-21. doi: 10.1111/j.1530-0277.2010.01269.x. Epub 2010 Jul 20.

53) THE IMPACT OF MATERNAL AGE ON THE EFFECTS OF PRENATAL ALCOHOL EXPOSURE ON ATTENTION.
Chiodo LM, da Costa DE, Hannigan JH, Covington CY, Sokol RJ, Janisse J, Greenwald M, Ager J, Delaney-Black V.
College of Nursing, Wayne State University, Detroit, Michigan 48201, USA. lchiodo@med.wayne.edu

ABSTRACT
Background: Prenatal exposure to alcohol has a variety of morphologic and neurobehavioral consequences, yet more than 10% of women continue to drink during pregnancy, placing their offspring at risk for fetal alcohol spectrum disorders (FASD). Identification of at-risk pregnancies has been difficult, in part, because the presence and severity of FASD are influenced by factors beyond the pattern of alcohol consumption. Establishing maternal characteristics, such as maternal age, that increase the risk of FASD is critical for targeted pregnancy intervention.

Methods: We examined the moderating effect of maternal age on measures of attention in 462 children from a longitudinal cohort born to women with known alcohol consumption levels (absolute ounces of alcohol per day at conception) who were recruited during pregnancy. Analyses examined the impact of binge drinking, as average ounces of absolute alcohol per drinking day. Smoking and use of cocaine, marijuana, and opiates were also assessed. At 7 years of age, the children completed the Continuous Performance Test, and their teachers completed the Achenbach Teacher Report Form.

Results: After controlling for covariates, stepwise multiple regression analyses revealed a negative relation between levels of prenatal binge drinking and several measures of attention. The interaction between alcohol consumption and maternal age was also significant, indicating that the impact of maternal binge drinking during pregnancy on attention was greater among children born to older drinking mothers.

Conclusion: These findings are consistent with previous findings that children born to older alcohol-using women have more deleterious effects of prenatal alcohol exposure on other neurobehavioral outcomes.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20645933

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PubMed, Int J Pediatr. 2010;2010. pii: 639048. Epub 2010 Jul 14.

54) SLEEP HEALTH ISSUES FOR CHILDREN WITH FASD: CLINICAL CONSIDERATIONS

James E. Jan,[1] Kwadwo O. Asante,[2] Julianne L. Conry,[3] Diane K. Fast,[4] Martin C. O. Bax,[5] Osman S. Ipsiroglu,[6] Elizabeth Bredberg,[7] Christine A. Loock,[6] and Michael B. Wasdell[7, 8]
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8Research Administration and Development, Fraser Health Authority, Surrey, BC, Canada V3R 7P8
Academic Editor: Myron Genel

ABSTRACT

This article describes the combined clinical experience of a multidisciplinary group of professionals on the sleep disturbances of children with fetal alcohol spectrum disorders (FASD) focusing on sleep hygiene interventions. Such practical and comprehensive information is not available in the literature. Severe, persistent sleep difficulties are frequently associated with this condition but few health professionals are familiar with both FASD and sleep disorders. The sleep promotion techniques used for typical children are less suitable for children with FASD who need individually designed interventions. The types, causes, and adverse effects of sleep disorders, the modification of environment, scheduling and preparation for sleep, and sleep health for their caregivers are discussed. It is our hope that parents and also researchers, who are interested in the sleep disorders of children with FASD, will benefit from this presentation and that this discussion will stimulate much needed evidence-based research.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2913852/?tool=pubmed

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NeuroReport – For Rapid Communication of Neuroscience Research
14 July 2010 - Volume 21 - Issue 10 - pp 716-721

55) FETAL BRAIN DURING A BINGE DRINKING EPISODE: A DYNAMIC SUSCEPTIBILITY CONTRAST MRI FETAL BRAIN PERFUSION STUDY

Kochunov, Peter

ABSTRACT

We assessed the effects of a single episode of maternal alcohol intoxication on fetal brain blood perfusion in three pregnant dams (baboons) at the 24th week of pregnancy using dynamic susceptibility contrast magnetic resonance imaging. After the oral administration of alcohol, there was a four-fold increase in the peak contrast concentrations in the fetal brain. In addition, we observed a two- to three-fold increase in the contrast uptake and washout rates in the fetal brain. The underlying mechanisms of these changes are unknown, but we hypothesized that these could include the alcohol-mediated changes in placental permeability and fetal cerebral blood flow. Our findings indicate that alcohol intoxication produces profound changes, which may detrimentally influence neurodevelopmental processes in the brain.

Read Full Article,
http://journals.lww.com/neuroreport/pages/articleviewer.aspx?year=2010&issue=07140&article=00010&type=abstract

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PubMed, Eur J Neurol. 2010 Jul 12. [Epub ahead of print]

56) GOAL-DIRECTED ARM MOVEMENTS IN CHILDREN WITH FETAL ALCOHOL SYNDROME: A KINEMATIC APPROACH.

Domellöf E, Fagard J, Jacquet AY, Rönnqvist L.
Department of Psychology, Umeå University, Umeå, Sweden.

ABSTRACT

Background: Although many studies have documented deficits in general motor functioning in children with fetal alcohol syndrome (FAS), few have employed detailed measurements to explore the specific nature of such disabilities. This pilot study explores whether three-dimensional (3D) kinematic analysis may generate increased knowledge of the effect of intrauterine alcohol exposure on motor control processes by detecting atypical upper-limb movement pattern specificity in children with FAS relative to typically developing (TD) children.

Methods: Left and right arm and head movements during a sequential unimanual goal-directed precision task in a sample of children with FAS and in TD children were registered by an optoelectronic tracking system (ProReflex, Qualisys Inc.).

Results: Children with FAS demonstrated evidently poorer task performance compared with TD children. Additionally, analyses of arm movement kinematics revealed atypical spatio-temporal organization in the children with FAS. In general, they exhibited longer arm movement trajectories at both the proximal and distal level, faster velocities at the proximal level but slower at the distal level, and more segmented distal movements. Children with FAS also showed atypically augmented and fast head movements during the task performance.

Conclusions: Findings indicate neuromotor deficits and developmental delay in goal-directed arm movements because of prenatal alcohol exposure. It is suggested that 3D kinematic analysis is a valid

technique for furthering the understanding of motor control processes in children with FAS/fetal alcohol spectrum disorders. A combination with relevant neuroimaging techniques in future studies would enable a more clear-cut interpretation of how atypical movement patterns relate to underlying brain abnormalities.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20629717

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PubMed, Alcohol Clin Exp Res. 2010 Oct;34(10):1793-802. doi: 10.1111/j.1530-0277.2010.01266.x. Epub 2010 Jul 9.

57) EFFECTS OF A NOVEL COGNITION-ENHANCING AGENT ON FETAL ETHANOL-INDUCED LEARNING DEFICITS

Savage DD, Rosenberg MJ, Wolff CR, Akers KG, El-Emawy A, Staples MC, Varaschin RK, Wright CA, Seidel JL, Caldwell KK, Hamilton DA.
Department of Neurosciences, MSC08 4740, 1 University of New Mexico, Albuquerque, NM 87131-0001, USA. dsavage@salud.unm.edu

ABSTRACT

Background: Drinking during pregnancy has been associated with learning disabilities in affected offspring. At present, there are no clinically effective pharmacotherapeutic interventions for these learning deficits. Here, we examined the effects of ABT-239, a histamine H_3 receptor antagonist, on fetal ethanol-induced fear conditioning and spatial memory deficits.

Methods And Results: Long-Evans rat dams stably consumed a mean of 2.82 g ethanol/kg during a 4-hour period each day during pregnancy. This voluntary drinking pattern produced a mean peak serum ethanol level of 84 mg/dl. Maternal weight gain, litter size and birth weights were not different between the ethanol-consuming and control groups. Female adult offspring from the control and fetal alcohol-exposed (FAE) groups received saline or 1 mg ABT-239/kg 30 minutes prior to fear conditioning training. Three days later, freezing time to the context was significantly reduced in saline-treated FAE rats compared to control. Freezing time in ABT-239-treated FAE rats was not different than that in controls. In the spatial navigation study, adult male offspring received a single injection of saline or ABT-239 30 minutes prior to 12 training trials on a fixed platform version of the Morris Water Task. All rats reached the same performance asymptote on Trials 9 to 12 on Day 1. However, 4 days later, first-trial retention of platform location was significantly worse in the saline-treated FAE rats compared control offspring. Retention by ABT-239-treated FAE rats was similar to that by controls. ABT-239's effect on spatial memory retention in FAE rats was dose dependent.

Conclusions: These results suggest that ABT-239 administered prior to training can improve retention of acquired information by FAE offspring on more challenging versions of hippocampal-sensitive learning tasks. Further, the differential effects of ABT-239 in FAE offspring compared to controls raises questions about the impact of fetal ethanol exposure on histaminergic neurotransmission in affected offspring.

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http://www.ncbi.nlm.nih.gov/pubmed/20626729

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Wiley Online Library - Synapse - Article first published online: 8 JUL 2010

58) SIRNA-MEDIATED GABAB RECEPTOR AT EARLY FETAL RAT BRAIN UPON ACUTE AND CHRONIC ETHANOL EXPOSURE: DOWN REGULATION OF PKA AND P-CREB EXPRESSION

M.I. Naseer, H.Y. Lee, N. Ullah, I. Ullah, M.S. Park, M.O. Kim

ABSTRACT

To observe the modulatory role of GABAB1R upon ethanol's effect during early brain development, we studied the effects of chronic maternal (10% ethanol during pregnancy) and acute (in vitro) ethanol exposure on the neuronal protein kinase A (PKA-α) and phosphorylation of cAMP-response element binding protein (p-CREB), using a system where GABAB1R were specifically knocked down in the primary cells cultured at gestational day (GD) 12.5. The results showed that upon acute and chronic ethanol treatment the GABAB1R expression was decreased and further decreased when GABAB1R was transfection with siRNA, while increased upon exposure of baclofen, and baclofen plus phaclofen treatment. PKA expression was also decreased with acute and chronic ethanol treatment, whereas it showed increase upon exposure of baclofen and baclofen with phaclofen. Furthermore, intracellular Ca2+ concentration was increased upon ethanol, baclofen, phaclofen exposure but showed decrease in GABAB1R siRNA group. Finally, these effects could lead to changes of p-CREB expression, which showed same expression pattern as PKA. We speculate that GABABR activity upon ethanol exposure could modulate intracellular calcium homeostasis and the expressional changes of PKA and p-CREB, which cause various negative effects on fetal brain development and modulation of GABABR upon ethanol exposure may underlying cause of ethanol's effects.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1002/syn.20824/abstract

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PubMed, Neurotoxicol Teratol. 2010 Jul 6. [Epub ahead of print]

59) CAUDATE ASYMMETRY: A NEUROBIOLOGICAL MARKER OF MODERATE PRENATAL ALCOHOL EXPOSURE IN YOUNG ADULTS

Willford J, Day R, Aizenstein H, Day N.
Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA.

ABSTRACT

This study identified structural changes in the caudate nucleus in offspring of mothers who drank moderate levels of alcohol during pregnancy. In addition, the effect of duration of alcohol use during pregnancy was assessed. Young adults were recruited from the Maternal Health Practices and Child Development Project. Three groups were evaluated: prenatal alcohol exposure (PAE) during all three trimesters (3T), PAE during the first trimester only (1T), and controls with no PAE (0T). Magnetic resonance images were processed using the automated labeling pathway technique. Volume was measured as the number (gray+white) and relative percentage (caudate count/whole brain countx100) of voxels. Asymmetry was calculated by subtracting the caudate volume on the left from the right and dividing by the total (L-R/L+R). Data analyses controlled for gender, handedness, and prenatal tobacco and marijuana exposures.

There were no significant differences between the groups for whole brain, left, or right volumes. There was a dose-response effect across the three exposure groups both in terms of magnitude and direction of asymmetry. In the 3T group, the left caudate was larger relative to the right caudate compared to the 0T group. The average magnitude of caudate asymmetry for the 1T group was

intermediate between the 0T and 3T groups. Subtle anatomical changes in the caudate are detected at the moderate end of the spectrum of prenatal alcohol exposure.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20609385

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PubMed, Alcohol Clin Exp Res. 2010 Oct;34(10):1705-13. doi: 10.1111/j.1530-0277.2010.01257.x. Epub 2010 Jul 5.

60) **THE INTERACTION OF GESTATIONAL AND POSTNATAL ETHANOL EXPERIENCE ON THE ADOLESCENT AND ADULT ODOR-MEDIATED RESPONSES TO ETHANOL IN OBSERVER AND DEMONSTRATOR RATS.**

Eade AM, Youngentob SL.
Department of Neuroscience and Physiology, State University of New York Upstate Medical University, Syracuse, New York 13210, USA.

ABSTRACT

Background: Gestational ethanol exposure enhances the adolescent reflexive sniffing response to ethanol odor. Postnatal exposures of naïve animals as either an observer (i.e., conspecific) or demonstrator (i.e., intoxicated peer) using a social transmission of food odor preference paradigm also yields enhanced odor-mediated responses. Studies on the interaction of fetal and postnatal exposures using the social transmission paradigm have been limited to the responses of observers. When combined, the enhanced response is greater than either form of exposure alone and, in observer females, yields adult persistence.
The absence of a male effect is noteworthy, given that chemosensory mechanisms are suggested to be an important antecedent factor in the progression of ethanol preference. Observers gain odor information on the breath of the demonstrator through social interaction. Demonstrators experience the pharmacologic properties of ethanol along with retronasal and hematogenic olfaction. Thus, we tested whether augmentation of the fetal ethanol-induced behavioral response with postnatal exposure as a demonstrator differed from that as an observer. We also examined whether re-exposure as a demonstrator yields persistence in both sexes.

Methods: Pregnant dams were fed an ethanol containing or control liquid diet throughout gestation. Progeny received four ethanol or water exposures: one every 48 hours through either intragastric infusion or social interaction with the infused peer beginning on P29. The reflexive behavioral sniffing response to ethanol odor was tested at postnatal (P) day 37 or P90, using whole-body plethysmography.

Results: When tested in either adolescence or adulthood - fetal ethanol exposed adolescent ethanol observers and demonstrators significantly differed in their odor-mediated response to ethanol odor both between themselves and from their respective water controls. Nonetheless, adolescent ethanol re-exposure as a demonstrator, like an observer, enhanced the reflexive sniffing response to ethanol odor at both testing ages by augmenting the known effects of prior fetal ethanol experience. At each age, the magnitude of the enhanced odor response in demonstrators was similar to that of observers. Interestingly, only re-exposure as a demonstrator resulted in persistence of the behavioral response into adulthood in both sexes.

Conclusions: The method of ethanol re-exposure plays an important role in prolonging the odor-mediated effects of fetal exposure. While ethanol odor-specific exposure through social interaction is

important, additional factors such as the pairing of retronasal and hematogenic olfaction with ethanol's intoxicating properties appear necessary to achieve persistence in both sexes.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20608909

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PubMed, Alcohol Clin Exp Res. 2010 Oct;34(10):1714-22. doi: 10.1111/j.1530-0277.2010.01258.x. Epub 2010 Jul 5.

61) ETHANOL ALTERS THE OSTEOGENIC DIFFERENTIATION OF AMNIOTIC FLUID-DERIVED STEM CELLS.

Hipp JA, Hipp JD, Atala A, Soker S.
Wake Forest Institute for Regenerative Medicine, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157, USA.

ABSTRACT
Background: Fetal alcohol spectrum disorder (FASD) is a set of developmental defects caused by prenatal alcohol exposure. Clinical manifestations of FASD are highly variable and include mental retardation and developmental defects of the heart, kidney, muscle, skeleton, and craniofacial structures. Specific effects of ethanol on fetal cells include induction of apoptosis as well as inhibition of proliferation, differentiation, and migration. This complex set of responses suggests that a bioinformatics approach could clarify some of the pathways involved in these responses.

Methods: In this study, the responses of fetal stem cells derived from the amniotic fluid (AFSCs) to treatment with ethanol have been examined. Large-scale transcriptome analysis of ethanol-treated AFSCs indicates that genes involved in skeletal development and ossification are up-regulated in these cells. Therefore, the effect of ethanol on osteogenic differentiation of AFSCs was studied.

Results: Exposure to ethanol during the first 48 hours of an osteogenic differentiation protocol increased in vitro calcium deposition by AFSCs and increased alkaline phosphatase activity. In contrast, ethanol treatment later in the differentiation protocol (day 8) had no significant effect on the activity of alkaline phosphatase.

Conclusions: These results suggest that transient exposure of AFSCs to ethanol during early differentiation enhances osteogenic differentiation of the cells.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20608908

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PubMed, Alcohol. 2010 Jun;44(4):371-8. Epub 2010 Jul 3.

62) MOTOR RESPONSE PROGRAMMING AND MOVEMENT TIME IN CHILDREN WITH HEAVY PRENATAL ALCOHOL EXPOSURE

Simmons RW, Thomas JD, Levy SS, Riley EP.
San Diego State University, CA 92182, USA. rsimmons@mail.sdsu.edu

ABSTRACT
The present experiment assessed motor response programming and movement time in children with histories of heavy prenatal alcohol exposure (PEA). Alcohol-exposed children between the ages of 7

and 17 years were classified into two groups: Fetal Alcohol Syndrome (FAS: n=9) and children with PEA (PEA: n=19) but who did not have the defining characteristics of FAS. The FAS and PEA children were compared with non-alcohol-exposed children (NC: n=23) when completing two tasks: a simple reaction time task (RT alone condition) and a reaction plus movement task (RT+Move condition). The movement involved responding to an imperative stimulus signal and depressing three target buttons in a set sequence. Participants completed 24 trials each for the RT alone and RT+Move response conditions. Results indicated no significant differences in performance among FAS, PEA, and NC groups during the RT alone condition. However, during the RT+Move condition, the FAS group produced significantly longer and more variable RTs than the PEA and NC groups, which produced comparable RTs. The FAS group also produced significantly slower movement times when moving to all three targets, whereas movement time variability did not significantly differ as a function of group. The observed results indicate children with FAS experience deficits in response programming and movement time production.

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http://www.ncbi.nlm.nih.gov/pubmed/20598488

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Wiley Online Library - Alcoholism: Clinical and Experimental Research, Volume 34, Issue 10, pages 1723–1732, October 2010. Article first published online: 1 JUL 2010

63) ACUTE AND CHRONIC ALCOHOL EXPOSURE IMPAIR THE PHAGOCYTOSIS OF APOPTOTIC CELLS AND ENHANCE THE PULMONARY INFLAMMATORY RESPONSE

Darren M. Boé, Tiffany R. Richens, Sarah A. Horstmann, Ellen L. Burnham, William J. Janssen, Peter M. Henson, Marc Moss, R. William Vandivier

ABSTRACT

Background: Alcohol abuse increases the risk for acute respiratory distress syndrome (ARDS). Efferocytosis, the clearance of apoptotic cells, is important in the resolution of inflammation and is regulated by RhoA and rho kinase (ROCK) activation. The effects of alcohol on pulmonary Rho pathway activation and efferocytosis have not been determined. We hypothesize that acute and chronic alcohol exposure impair pulmonary efferocytosis, leading to heightened inflammation during ARDS.

Methods: For in vivo experiments, C57BL/6 mice received either a single intraperitoneal injection of alcohol or chronic ethanol-in-water for 8 weeks prior to intratracheal instillation of apoptotic cells or lipopolysaccharide (LPS). Bronchoalveolar lavage (BAL) was performed for cells counts, calculation of the phagocytic index (PI), and Rho activity measurements. For in vitro studies, primary alveolar macrophages were cultured in alcohol (25–100 mM) and then co-cultured with apoptotic cells. RhoA activity was determined following alcohol exposure, and the PI was determined before and after treatment with the ROCK inhibitor, Y27632.

Results: Acute alcohol exposure was associated with impaired efferocytosis. Following LPS exposure, acute alcohol exposure was also associated with increased BAL neutrophils. Chronic alcohol exposure alone did not alter efferocytosis. However, following exposure to LPS, chronic alcohol exposure was associated with both impaired efferocytosis and increased BAL neutrophils. In vitro alcohol exposure caused a dose-dependent decrease in efferocytosis. Despite the fact that RhoA activity was decreased by alcohol exposure and RhoA inhibition did not alter the effects of alcohol on efferocytosis, treatment with the Rho kinase inhibitor, Y27632, reversed the effects of alcohol on efferocytosis.

Conclusions: Acute alcohol exposure impairs pulmonary efferocytosis, whereas exposure to chronic alcohol is only associated with impaired efferocytosis following LPS-induced lung injury. Both forms of alcohol exposure are associated with increased alveolar neutrophil numbers in response to LPS. The acute effects of alcohol on efferocytosis appear to be mediated, at least in part, by RhoA-independent activation of ROCK.

Further studies are needed to dissect the differences between the effects of acute and chronic alcohol exposure on efferocytosis and to determine the effects of alcohol on alternative activators of ROCK.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1111/j.1530-0277.2010.01259.x/abstract

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PubMed, J Am Osteopath Assoc. 2010 Jul;110(7):381-4.

64) USING ONE QUESTION TO IDENTIFY WOMEN AT RISK FOR AN ALCOHOL-EXPOSED PREGNANCY

Johnson KE, Sobell MB, Sobell LC.
College of Osteopathic Medicine, Health Professions Division, Nova Southeastern University, Fort Lauderdale, FL 33314-7721, USA.

ABSTRACT

Context: Consumption of 8 alcoholic drinks per week or 5 alcoholic drinks on one occasion by a pregnant woman can affect the developing fetus. However, it can be difficult to determine which patients are at risk.

Objective: To evaluate how well the answer to a single question about binge drinking could help identify women at risk of an alcohol-exposed pregnancy (AEP).

Methods: Using data from a study of methods to prevent AEPs, the authors compared the efficacy of self-reported answers to a screening question about binge drinking (5 or more standard drinks on one occasion) within the past 90 days with answers to a question about drinking quantity (weekly consumption of 8 or more standard drinks) within the past 90 days.

Results: The participants were 354 women of childbearing age who met screening criteria for being at risk of an AEP. The binge question was answered positively by 346 women (97.7%) at risk, while only 209 women (59.0%) reported that they drank 8 or more drinks in a week.

Conclusion: A single question about binge drinking can effectively and quickly identify the majority of women at risk of an AEP.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20693570

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PubMed, Yao Xue Xue Bao. 2010 Jul;45(7):833-9.

65) EFFECTS OF ALCOHOL EXPOSURE DURING PREGNANCY ON DENDRITIC SPINE AND SYNAPSE OF VISUAL CORTEX IN FILIAL MICE

Cui ZJ, Zhao KB, Wen SG, Zhang JS, Yu DM, Deng JB.
Institute of Neurobiology of Medical College of Henan University, Kaifeng 475004, China.

ABSTRACT
The prenatal ethanol exposure induced the alterations of dendritic spine and synapse in visual cortex and their long-term effect would be investigated in mice from P0 to P30. Pregnant mice were intubated ethanol daily from E5 through the pup's birth to establish mode of prenatal alcohol abuse. The dendritic spines of pyramidal cells in visual cortex of pups were labeled with DiI diolistic assay, and the synaptic ultrastructure was observed under transmission electron microscope. Prenatal alcohol exposure was associated with a significant decrease in the number of dendritic spines of pyramidal neurons in the visual cortex and an increase in their mean length; ultrastructural changes were also observed, with decreased numbers of synaptic vesicles, narrowing of the synaptic cleft and thickening of the postsynaptic density compared to controls. Prenatal alcohol exposure is associated with long-term changes in dendritic spines and synaptic ultrastructure. The changes were dose-dependent with long term effect even at postnatal 30.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20931779

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J Popul Ther Clin Pharmacol Vol 17 (2) Summer 2010:e269-e280; June 30, 2010

66) THE MOTHERISK ALCOHOL AND SUBSTANCE USE HELPLINE: 10 YEARS OF EXPERIENCE AND COUNTING

Eunji Kim, Moumita Sarkar, Yvette Navioz, Gideon Koren, Adrienne Einarson

ABSTRACT
The Motherisk Alcohol and Substance Use Helpline at The Hospital for Sick Children in Toronto, Canada, is a unique telephone service providing evidence-based information on the negative effects associated with alcohol and substance use in pregnancy and lactation. We describe the characteristics of the service, the demographics of the callers, and the inquiries made during its first ten years of service. Since its inception in November 1998 until November 2008, almost 20,000 calls had been received with 60% of calls initiated by pregnant and breastfeeding women, the remainder from various health care providers. Most women exposed to alcohol and substances were of Caucasian descent (80%), employed (65%), and married (46%) with some level of post-secondary education (52%). The demographics of the callers deviate from the well-documented cohort of women at risk of engaging in alcohol and substance use in pregnancy and lactation, confirming that a selective group of women is more likely to use the services offered by the Motherisk program. Thus, further efforts are required to reach out to the subgroup of women at high risk of continuing their harmful behaviors during pregnancy and lactation.

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http://www.cjcp.ca/pubmed.php?articleId=269

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PubMed, Alcohol. 2010 Jun 30. [Epub ahead of print]

67) IMPACT OF PRENATAL ALCOHOL CONSUMPTION ON PLACENTA-ASSOCIATED SYNDROMES

Salihu HM, Kornosky JL, Lynch O, Alio AP, August EM, Marty PJ.
The Chiles Center for Healthy Mothers and Babies, University of South Florida, Tampa, FL 33612, USA; Department of Epidemiology and Biostatistics, University of South Florida, Tampa, FL 33612, USA; Department of Obstetrics and Gynecology, University of South Florida, Tampa, FL 33612, USA.

ABSTRACT
The biology of placental and fetal development suggests that alcohol may play a significant role in increasing the risk of feto-infant morbidity and mortality, but study results are inconsistent and the mechanism remains poorly defined. Previous studies have not examined the risk of placenta-associated syndromes (PASs: defined as the occurrence of either placental abruption, placenta previa, preeclampsia, small for gestational age, preterm, or stillbirth) as a unique entity. Therefore, we sought to examine the relationship between prenatal alcohol use and the risk of PAS among singleton births in the Missouri maternally linked data files covering the period 1989-2005. Logistic regression with adjustment for intracluster correlation was used to generate adjusted odds ratios (ORs) and 95% confidence intervals (CIs). Compared with nondrinkers, drinkers were more likely to be smokers, 35 years of age or older, black, and multiparous. Drinkers had an increased risk of PAS (OR=1.26, 95% CI=1.22,1.31) when compared with their nondrinking counterparts. The risk of PAS was progressively amplified with increasing prenatal alcohol consumption (P for trend <.01). Women who reported consuming five or more alcoholic drinks per week had more than twofold increased risk of PASs, whereas women in the lowest drinking category (one to two drinks per week) had only a slight increased risk of PAS (OR=1.09, 95% CI=1.05, 1.14). Enhanced understanding of the mechanism by which prenatal alcohol consumption leads to PAS may aid in the development of more targeted interventions designed to prevent adverse pregnancy outcomes. Screening women for alcohol use may assist providers in protecting developing fetuses from the potential dangers of prenatal alcohol use.

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http://www.ncbi.nlm.nih.gov/pubmed/20598485

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PubMed, Neurotoxicol Teratol. 2010 Jun 30. [Epub ahead of print]

68) EFFECTS OF PRENATAL TOBACCO, ALCOHOL AND MARIJUANA EXPOSURE ON PROCESSING SPEED, VISUAL-MOTOR COORDINATION, AND INTERHEMISPHERIC TRANSFER

Willford JA, Chandler LS, Goldschmidt L, Day NL.
Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213, USA.

ABSTRACT
Deficits in motor control are often reported in children with prenatal alcohol exposure (PAE). Less is known about the effects of prenatal tobacco exposure (PTE) and prenatal marijuana exposure (PME) on motor coordination, and previous studies have not considered whether PTE, PAE, and PME interact to affect motor control. This study investigated the effects of PTE, PAE, and PME as well as current drug use on speed of processing, visual-motor coordination, and interhemispheric transfer in 16-year-old adolescents. Data were collected as part of the Maternal Health Practices and Child Development Project. Adolescents (age 16, n=320) participating in a longitudinal study of the effects

of prenatal substance exposure on developmental outcomes were evaluated in this study. The computerized Bimanual Coordination Test (BCT) was used to assess each domain of function. Other important variables, such as demographics, home environment, and psychological characteristics of the mother and adolescent were also considered in the analyses. There were significant and independent effects of PTE, PAE, and PME on processing speed and interhemispheric transfer of information. PTE and PME were associated with deficits in visual-motor coordination. There were no interactions between PAE, PTE, and PME. Current tobacco use predicted deficits in speed of processing. Current alcohol and marijuana use by the offspring were not associated with any measures of performance on the BCT.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20600845

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Hum Reprod. 2010 Sep;25(9):2340-5. Epub 2010 Jun 29.

69) MATERNAL ALCOHOL CONSUMPTION DURING PREGNANCY AND SEMEN QUALITY IN THE MALE OFFSPRING: TWO DECADES OF FOLLOW-UP

Ramlau-Hansen CH, Toft G, Jensen MS, Strandberg-Larsen K, Hansen ML, Olsen J.
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ABSTRACT

Background: Concurrent alcohol exposure has been associated with reduced fecundity, but no studies have estimated the effect of prenatal alcohol exposure on male fecundity. The aim of this study was to investigate the association between maternal alcohol consumption during pregnancy, semen quality and levels of reproductive hormones in young, adult men.

Methods: From a Danish pregnancy cohort established in 1984-1987, 347 sons were selected for a follow-up study conducted in 2005-2006. Semen and blood samples were analyzed for conventional semen characteristics and reproductive hormones, respectively, and results were related to prospectively self-reported information on maternal alcohol consumption during pregnancy.

Results: The sperm concentration decreased with increasing prenatal alcohol exposure. The adjusted mean sperm concentration among sons of mothers drinking >or=4.5 drinks per week during pregnancy was 40 (95% CI: 25-60) millions/ml. This concentration was approximately 32% lower compared with men exposed to <1.0 drink per week, who had a sperm concentration of 59 (95% CI: 44-77) millions/ml. The semen volume and the total sperm count were also associated with prenatal alcohol exposure; sons prenatally exposed to 1.0-1.5 drinks per week had the highest values. No associations were found for sperm motility, sperm morphology or any of the reproductive hormones, including testosterone.

Conclusions: These results indicate that prenatal exposure to alcohol may have a persisting adverse effect on Sertoli cells, and thereby sperm concentration. If these associations are causal they could explain some of the reported differences between populations and long-term changes in semen quality.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20587536

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PubMed, Front Neurosci. 2010; 4: 41. Published online 2010 June 28.

70) LITHIUM-MEDIATED PROTECTION AGAINST ETHANOL NEUROTOXICITY

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Reviewed by: Jordi Calderó, Universitat de Lleida and Institut de Recerca Biomedica de Lleida, Spain; Xiao-Ming Ou, University of Mississippi Medical Center, USA

ABSTRACT

Lithium has long been used as a mood stabilizer in the treatment of manic-depressive (bipolar) disorder. Recent studies suggest that lithium has neuroprotective properties and may be useful in the treatment of acute brain injuries such as ischemia and chronic neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease and amyotrophic lateral sclerosis. One of the most important neuroprotective properties of lithium is its anti-apoptotic action. Ethanol is a neuroteratogen and fetal alcohol spectrum disorders (FASD) are caused by maternal ethanol exposure during pregnancy. FASD is the leading cause of mental retardation. Ethanol exposure causes neuroapoptosis in the developing brain. Ethanol-induced loss of neurons in the central nervous system underlies many of the behavioral deficits observed in FASD. Excessive alcohol consumption is also associated with Wernicke–Korsakoff syndrome and neurodegeneration in the adult brain. Recent in vivo and in vitro studies indicate that lithium is able to ameliorate ethanol-induced neuroapoptosis. Lithium is an inhibitor of glycogen synthase kinase 3 (GSK3) which has recently been identified as a mediator of ethanol neurotoxicity. Lithium's neuroprotection may be mediated by its inhibition of GSK3. In addition, lithium also affects many other signaling proteins and pathways that regulate neuronal survival and differentiation. This review discusses the recent evidence of lithium-mediated protection against ethanol neurotoxicity and potential underlying mechanisms.

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2907128/?tool=pubmed

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PubMed, Alcohol. 2010 Jun 26. [Epub ahead of print]

71) RATES OF FETAL ALCOHOL EXPOSURE AMONG NEWBORNS IN A HIGH-RISK OBSTETRIC UNIT.

Goh YI, Hutson JR, Lum L, Roukema H, Gareri J, Lynn H, Koren G.
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ABSTRACT

Meconium fatty acid ethyl esters (FAEEs) are sensitive and specific biomarkers for prenatal alcohol exposure (PAE) in pregnancy. We recently reported a 2.5% rate of FAEE positive meconium in a general population sample of infants born in the region of Grey-Bruce, Ontario. Women in this region with high-risk pregnancies are transferred to a tertiary care facility in London, Ontario. The objective of this study was to determine, in a population-based sample, whether high-risk pregnancies are associated with an increased risk of in utero alcohol exposure. Grey-Bruce residents transferred to the high-risk obstetric unit of St. Joseph's Health Care in London, Ontario were identified and consented to this anonymous prevalence study. Meconium was collected and analyzed for FAEE using gas chromatography with mass spectrometry. The prevalence of FAEE positive meconium was compared with the population-based prevalence in the Grey-Bruce. Fifty meconium specimens were collected

from August 1, 2006 to July 31, 2007. Fifteen (30%) specimens tested positive for FAEE. The results indicate that infants born in the high-risk obstetric unit had a 12-fold higher risk of screening positive for second and third trimester alcohol exposure compared with infants born in the general population of Grey-Bruce (relative risk=12.04, 95% confidence interval=6.40-22.65, P<.0001). These results suggest that the high-risk pregnancies should be screened for PAE and followed-up for potential diagnosis of fetal alcohol spectrum disorder.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20584588

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Alcohol Clin Exp Res. 2010 Sep 1;34(9):1574-83. Epub 2010 Jun 25.

72) ETHANOL ALTERS CELL FATE OF FETAL HUMAN BRAIN-DERIVED STEM AND PROGENITOR CELLS

Vangipuram SD, Lyman WD.
Children's Research Center of Michigan, The Carman and Ann Adams Department of Pediatrics, Wayne State University School of Medicine and Children's Hospital of Michigan, Detroit, Michigan 48201, USA. svangipuram@med.wayne.edu

ABSTRACT

Background: Prenatal ethanol (ETOH) exposure can lead to fetal alcohol spectrum disorder (FASD). We previously showed that ETOH alters cell adhesion molecule gene expression and increases neurosphere size in fetal brain-derived neural stem cells (NSC). Here, our aim was to determine the effect of ETOH on the cell fate of NSC, premature glial-committed precursor cells (GCP), and premature neuron-committed progenitor cells (NCP).

Methods: NSC, GCP, and NCP were isolated from normal second-trimester fetal human brains (n = 3) by positive selection using magnetic microbeads labeled with antibodies to CD133 (NSC), A2B5 (GCP), or PSA-NCAM (NCP). As a result of the small percentage in each brain, NSC were cultured in mitogenic media for 72 hours to produce neurospheres. The neurospheres from NSC and primary isolates of GCP and NCP were used for all experiments. Equal numbers of the 3 cell types were treated either with mitogenic media or with differentiating media, each containing 0 or 100 mM ETOH, for 120 hours. Expression of Map2a, GFAP, and O4 was determined by immunoflourescence microscopy and western blot analysis. Fluorescence intensities were quantified using Metamorph software by Molecular Devices, and the bands of western blots were quantified using densitometry.

Results: ETOH in mitogenic media promoted formation of neurospheres by NSC, GCP, and NCP. Under control conditions, GCP attached and differentiated, NSC and NCP formed neurospheres that were significantly smaller in size than those in ETOH. Under differentiating conditions, Map2a expression increased significantly in NSC and GCP and reduced significantly in NCP, and GFAP expression reduced significantly in GCP and NCP, and Gal-C expression reduced significantly in all 3 cell types in the presence of ETOH compared to controls.

Conclusions: This study shows that ETOH alters the cell fate of neuronal stem and progenitor cells. These alterations could contribute to the mechanism for the abnormal brain development in FASD.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20586756

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PubMed, Alcohol. 2010 Jun 24. [Epub ahead of print]

73) CORRELATION BETWEEN DRUGS OF ABUSE AND ALCOHOL BY HAIR ANALYSIS: PARENTS AT RISK FOR HAVING CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDER

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ABSTRACT
The fatty acid ethyl esters (FAEEs) hair test, a biomarker of excessive alcohol exposure, has demonstrated its potential for use in fetal alcohol spectrum disorder (FASD) diagnosis. FASD may be compounded by polydrug exposure. Our objective was to determine the likelihood of positive FAEE test among parents testing positive for other drugs of abuse. Samples submitted for FAEE hair analysis by Children's Aid Societies between October 2005 and May 2007, also concurrently tested for cocaine, cannabinoids, opiates, methamphetamine, amphetamine, benzodiazepines, methadone, and/or oxycodone, were included in our analysis. Subjects consisted of parents suspected of using excessive amounts of alcohol. Parents testing positive for drugs of abuse had a significantly increased risk for testing positive for high FAEE. Mothers testing positive for heavy chronic alcohol use were found to have a threefold increased risk of testing positive for cocaine (odds ratio=3.26, 1.1-9.7). Our results suggest that parents abusing stimulants are at risk of high alcohol exposure, which put their unborn children at risk for FASD.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20580184

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Alcohol Clin Exp Res. 2010 Sep 1;34(9):1640-50. Epub 2010 Jun 21.

74) TOWARD A NEUROBEHAVIORAL PROFILE OF FETAL ALCOHOL SPECTRUM DISORDERS.

Mattson SN, Roesch SC, Fagerlund A, Autti-Rämö I, Jones KL, May PA, Adnams CM, Konovalova V, Riley EP; Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD).
Center for Behavioral Teratology, San Diego State University, San Diego, California, USA.

ABSTRACT
Background: A primary goal of recent research is the development of neurobehavioral profiles that specifically define fetal alcohol spectrum disorders (FASD), which may assist differential diagnosis or improve treatment. In the current study, we define a preliminary profile using neuropsychological data from a multisite study.

Methods: Data were collected using a broad neurobehavioral protocol from 2 sites of a multisite study of FASD. Subjects were children with heavy prenatal alcohol exposure and unexposed controls. The alcohol-exposed group included children with and without fetal alcohol syndrome (FAS). From 547 neuropsychological variables, 22 variables were selected for analysis based on their ability to distinguish children with heavy prenatal alcohol exposure from nonexposed controls. These data were analyzed using latent profile analysis (LPA).

Results: The results indicated that a 2-class model best fit the data. The resulting profile was successful at distinguishing subjects with FAS from nonexposed controls without FAS with 92% overall accuracy; 87.8% of FAS cases and 95.7% of controls were correctly classified. The same

analysis was repeated with children with heavy prenatal alcohol exposure but without FAS and nonexposed controls with similar results. The overall accuracy was 84.7%; 68.4% of alcohol-exposed cases and 95% of controls were correctly classified. In both analyses, the profile based on neuropsychological variables was more successful at distinguishing the groups than was IQ alone.

Conclusions: We used data from 2 sites of a multisite study and a broad neuropsychological test battery to determine a profile that could be used to accurately identify children affected by prenatal alcohol exposure. Results indicated that measures of executive function and spatial processing are especially sensitive to prenatal alcohol exposure.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20569243

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PubMed, Med J Aust. 2010 Jun 21;192(12):690-3.

75) ASSESSING PREGNANT WOMEN'S COMPLIANCE WITH DIFFERENT ALCOHOL GUIDELINES: AN 11-YEAR PROSPECTIVE STUDY

Powers JR, Loxton DJ, Burns LA, Shakeshaft A, Elliott EJ, Dunlop AJ.
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ABSTRACT

Objective: To assess women's compliance with different Australian guidelines on alcohol intake during pregnancy and examine factors that might influence compliance.

Design, Setting And Participants: We analysed prospective, population-based data on women aged 22-33 years who were pregnant before October 2001, when guidelines recommended zero alcohol (n = 419), or were first pregnant after October 2001, when guidelines recommended low alcohol intake (n = 829). Data were obtained from surveys conducted in 1996, 2000, 2003 and 2006 as part of the Australian Longitudinal Study on Women's Health.

Main Outcome Measures: Relative risks (RRs) for zero alcohol intake, low alcohol intake and compliance with alcohol guidelines, estimated by a modified Poisson regression model with robust error variance.

Results: About 80% of women consumed alcohol during pregnancy under zero and low alcohol guidelines. Compliance with zero alcohol guidelines or low alcohol guidelines (up to two drinks per day and less than seven drinks per week) was the same for women who were pregnant before October 2001 and women who were first pregnant after October 2001 (20% v 17% for compliance with zero alcohol guidelines, P > 0.01; 75% v 80% for compliance with low alcohol guidelines, P > 0.01). Over 90% of women drank alcohol before pregnancy and prior alcohol intake had a strong effect on alcohol intake during pregnancy, even at low levels (RR for zero alcohol, 0.21 [95% CI, 0.16-0.28]; RR for low alcohol, 0.91 [95% CI, 0.86-0.96]).

RR for compliance with guidelines was 3.54 (95% CI, 2.85-4.40) for women who were pregnant while low alcohol intake was recommended, compared with those who were pregnant while zero alcohol guidelines were in place.

Conclusion: The October 2001 change in alcohol guidelines does not appear to have changed behaviour. Risks associated with different levels of alcohol intake during pregnancy need to be clearly established and communicated.

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http://www.ncbi.nlm.nih.gov/pubmed/20565346

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Sciencedirect. Available online 18 June 2010.

76) REDUCTION OF ETHANOL-INDUCED OCULAR ABNORMALITIES IN MICE THROUGH DIETARY ADMINISTRATION OF N-ACETYLCYSTEINE

Scott E. Parnell[a], Kathleen K. Sulik[a], Deborah B. Dehart[a] and Shao-yu Chen[b]
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b Department of Cancer Biology and Pharmacology, University of Illinois College of Medicine at Peoria, Peoria, IL, USA

ABSTRACT
N-Acetylcysteine (NAC) is a derivative of the amino acid l-cysteine, which, previously, has been shown to protect against ethanol-induced apoptosis during early development. Ongoing research demonstrates that NAC is also proving clinically beneficial in reducing oxidative stress–mediated lung, liver, and kidney damage, with protection likely resulting from a NAC-mediated increase in glutathione levels. In the present study, the hypothesis that coadministration of NAC and ethanol by means of liquid diet on days 7 and 8 of pregnancy in mice would reduce ethanol's teratogenicity was tested. For this work, adult nonpregnant female mice were acclimated to a liquid diet containing ethanol for 16 days, withdrawn from the ethanol, bred, and then returned to the liquid diet containing 4.8% ethanol and/or either 0.5 or 1-mg NAC/mL diet on their seventh and eighth days of pregnancy. At the concentrations used, the mice received NAC dosages of approximately 300 or 600 mg/kg/day and achieved peak blood ethanol concentrations (BEC) that averaged approximately 200 mg/dL. There was no difference in BEC between the ethanol-alone and ethanol plus 600 mg/kg NAC group. After maternal euthanasia, gestational day (GD) 14 fetuses were removed, fixed, weighed, and examined for the presence and severity of ocular abnormalities, a readily assessed endpoint that results from GD 7 and 8 ethanol exposures. Although the lower dosage of NAC (300 mg/kg) resulted in a decrease in the incidence of ocular defects in both the left and right eyes, this reduction was not statistically significant. However, doubling the NAC concentration did yield a significant change; as compared with the group treated with ethanol alone, the incidence of ocular abnormalities was diminished by 22%. These results show the potential of an orally administered compound with proven clinical efficacy to reduce ethanol's teratogenic effects and support the premise that oxidative damage plays an important mechanistic role in fetal alcohol spectrum disorders.

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http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T40-50BBSVH-4&_user=10&_coverDate=06/18/2010&_rdoc=1&_fmt=high&_orig=search&_origin=search&_sort=d&_docanchor=&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=8319db3fc0c0e9ebc8b22b996be310bf&searchtype=a

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PubMed, Dev Neurosci. 2010 Jul;32(2):91-100. Epub 2010 Jun 16.

77) SCREENING, DIAGNOSING AND PREVENTION OF FETAL ALCOHOL SYNDROME: IS THIS SYNDROME TREATABLE?

Ismail S, Buckley S, Budacki R, Jabbar A, Gallicano GI.
Department of Biochemistry and Molecular and Cellular Biology, Georgetown University Medical Center, Washington, D.C. 20057, USA.

ABSTRACT
Prenatal alcohol exposure can lead to a wide range of adverse effects on a developing fetus. As a whole, these teratogenic outcomes are generally known as fetal alcohol spectrum disorders, the most severe of which is fetal alcohol syndrome (FAS). Clinically, children diagnosed with FAS vary greatly in their presentation of symptoms, likely due to the amount of alcohol and timing of exposure, as well as maternal and genetic influences. All these factors play a role in determining the mechanisms through which alcohol damages a developing brain, the details of which are still largely unknown. However, continuing research and recent developments have provided promising results that may lead to screening mechanisms and treatment therapies for children with FAS. Here we review the teratogenic effects of alcohol, strategies for detecting maternal alcohol consumption, identification of fetal biological markers, and prevention methods for FAS.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20551645

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PubMed, Alcohol Alcohol. 2010 Jul-Aug;45(4):312-9. Epub 2010 Jun 11.

78) PRENATAL ALCOHOL EXPOSURE INDUCES LONG-TERM CHANGES IN DENDRITIC SPINES AND SYNAPSES IN THE MOUSE VISUAL CORTEX

Cui ZJ, Zhao KB, Zhao HJ, Yu DM, Niu YL, Zhang JS, Deng JB.
Institute of Neurobiology and Laboratory of Neurobiology, Henan University, Kaifeng, Henan Province, PR China.

ABSTRACT
Aims: To study the long-term changes of dendritic spine and synapse taking place in a mouse model of fetal alcohol spectrum disorders (FASDs).

Methods: Pregnant mice were intubated daily with ethanol (EtOH) from E5 to parturition. A DiI diolistic method was used to label dendritic spines of pyramidal cells in the visual cortex of EtOH-exposed and control pups over the period from postnatal (P) day P0 to P30; synaptic ultrastructure was also analyzed using transmission electron microscopy.

Results: Prenatal alcohol exposure was associated with a significant decrease in the number of dendritic spines of pyramidal neurons in the visual cortex and an increase in their mean length. The changes were dose dependent and persisted to P30. Ultrastructural changes were also observed, with decreased numbers of synaptic vesicles, narrowing of the synaptic cleft and thickening of the postsynaptic density compared to controls; ultrastructural changes also persisted to P30.

Conclusions: Prenatal alcohol exposure is associated with long-term changes in dendritic spines and synaptic ultrastructure; these alterations probably reflect the developmental retardation of dendritic spines and synapses in visual cortex.

These long-term changes are likely to contribute to lifelong mental retardation associated with childhood FASDs.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20543181

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Int J Neuropsychopharmacol. 2010 Sep;13(8):1053-66. Epub 2010 Jun 9.

79) EPIGALLOCATECHIN-3-GALLATE AMELIORATES ALCOHOL-INDUCED COGNITIVE DYSFUNCTIONS AND APOPTOTIC NEURODEGENERATION IN THE DEVELOPING RAT BRAIN

Tiwari V, Kuhad A, Chopra K.
Pharmacology Research Laboratory, University Institute of Pharmaceutical Sciences, UGC Center of Advanced Study, Panjab University, Chandigarh, India.

ABSTRACT
Clinical and experimental evidence has demonstrated that ethanol is a teratogen, and its consumption during pregnancy induces harmful effects on the developing fetus that leads to mental retardation and long-term cognitive and behavioural deficits in offspring. The brain growth spurt period is highly sensitive to the neurotoxic effects of ethanol and it corresponds to the last trimester in humans and the first two postnatal weeks in rodents. This study was designed to evaluate the effect of epigallocatechin-3-gallate (EGCG) on alcohol-induced behavioural, biochemical and molecular changes in rat pups. Pups were administered alcohol (5 g/kg, 12% v/v) by intragastric intubation on postnatal days (PD) 7, 8, and 9. Ethanol-exposed pups showed impaired spatial navigation in the Morris water maze test and poor retention in the elevated plus maze task conducted from PD 24 to 28 which was coupled with enhanced acetylcholinesterase activity, increased oxidative-nitrosative stress, cytokines (TNF-alpha and IL-1beta), NF-kappaB and caspase-3 levels in both the cortex and hippocampus of pups sacrificed at PD 28. Apart from this, the mean weight of the whole brain, cortex and hippocampus of ethanol-treated pups was decreased by 34.48%, 39.09% and 34.30%, respectively. EGCG (50 and 100 mg/kg) significantly attenuated all the behavioural, biochemical and molecular changes in the different brain regions of ethanol-treated pups. The current finding demonstrates the activation of oxidative-nitrosative stress-mediated apoptotic signalling in cognitive deficits associated with fetal alcohol spectrum disorders (FASDs) and suggests that EGCG may have potential in prevention of the cognitive impairment in children with FASDs.

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http://www.ncbi.nlm.nih.gov/pubmed/20529413

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PubMed, Alcohol Clin Exp Res. 2010 Aug;34(8):1450-64. Epub 2010 Jun 7.

80) AN FMRI STUDY OF NUMBER PROCESSING IN CHILDREN WITH FETAL ALCOHOL SYNDROME

Meintjes EM, Jacobson JL, Molteno CD, Gatenby JC, Warton C, Cannistraci CJ, Hoyme HE, Robinson LK, Khaole N, Gore JC, Jacobson SW.
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ABSTRACT
Background: Number processing deficits are frequently seen in children exposed to alcohol in utero.

Methods: Functional magnetic resonance imaging was used to examine the neural correlates of number processing in 15 right-handed, 8- to 12-year-old children diagnosed with fetal alcohol syndrome (FAS) or partial FAS (PFAS) and 18 right-handed, age- and gender-matched controls from the Cape Coloured (mixed ancestry) community in Cape Town, South Africa, using Proximity Judgment and Exact Addition tasks.

Results: Control children activated the expected fronto-parietal network during both tasks, including the anterior horizontal intraparietal sulcus (HIPS), left posterior HIPS, left precentral sulcus, and posterior medial frontal cortex. By contrast, on the Proximity Judgment task, the exposed children recruited additional parietal pathways involving the right and left angular gyrus and posterior cingulate/precuneus, which may entail verbally mediated recitation of numbers and/or subtraction to assess relative numerical distances. During Exact Addition, the exposed children exhibited more diffuse and widespread activations, including the cerebellar vermis and cortex, which have been found to be activated in adults engaged in particularly challenging number processing problems.

Conclusions: The data suggest that, whereas control children rely primarily on the fronto-parietal network identified in previous studies to mediate number processing, children with FAS/PFAS recruit a broader range of brain regions to perform these relatively simple number processing tasks. Our results are consistent with structural neuroimaging findings indicating that the parietal lobe is relatively more affected by prenatal alcohol exposure and provide the first evidence for brain activation abnormalities during number processing in children with FAS/PFAS, effects that persist even after controlling statistically for group differences in total intracranial volume and IQ.

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http://www.ncbi.nlm.nih.gov/pubmed/20528824

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PubMed, Alcohol. 2010 Jun 5. [Epub ahead of print]

81) ALCOHOL-INDUCED FACIAL DYSMORPHOLOGY IN C57BL/6 MOUSE MODELS OF FETAL ALCOHOL SPECTRUM DISORDER

Anthony B, Vinci-Booher S, Wetherill L, Ward R, Goodlett C, Zhou FC.
Department of Anatomy & Cell Biology, Indiana University School of Medicine, Indianapolis, IN 46202, USA.

ABSTRACT
Alcohol consumption during pregnancy causes fetal alcohol spectrum disorder (FASD), which includes a range of developmental deficits. Fetal alcohol syndrome is the most severe form of FASD and can be diagnosed with pathognomonic facial features such as a smooth philtrum, short palpebral fissure, and thin upper vermilion. However, many children with developmental damage because of prenatal alcohol exposure exhibit none, or only a subset, of the above features, making diagnosis difficult. This study explored novel analyses to quantify the effect of a known dose of alcohol on specific facial measurements in substrains C57BL/B6J (B6J) and C57BL/6NHsd (B6N) mice. Mouse dams were provided alcohol (Alc) consisting of 4.8% (vol/vol) alcohol in a liquid diet for 16 days prepregnancy and chow and water diet during mating, and then the alcohol liquid diet was reinstated on gestational days 7 (E7) to gestational day 17 (E17). Treatment controls included a pair-fed (PF) group given matched volumes of an alcohol-free liquid diet made isocalorically and a group given ad lib access to lab chow and water (Chow). Maternal diet intake (Alc and PF), blood alcohol concentrations (BACs), embryo weights, and 15 morphometric facial measurements for E17 embryos were analyzed. B6N dams drank more alcohol during pregnancy and generated higher BAC than B6J dams. Both the Alc and PF treatments induced significant reductions in embryo weights relative to Chow in both substrains.

Alcohol treatments produced significant changes, relative to controls, in 4 of the 15 facial measures for the B6N substrain but only in two measures for the B6J substrain. Discriminant analysis demonstrated successful classification of the alcohol-exposed versus nonalcohol-exposed B6N embryos, with a high sensitivity of 86%, specificity 80%, and overall classification (total correct 83%), whereas B6J mice yielded sensitivity of 80%, specificity 78%, and overall correct classification in 79%. In addition, B6N mice showed significantly more effects of pair feeding on these facial measures than did B6J mice, suggesting that the B6N substrain may be more vulnerable to nutritional stress during pregnancy. Overall, these data indicate that both B6N and B6J mice were vulnerable to alcohol but show differences in the severity and location of alcohol-induced dysmorphic facial features and may parallel findings from human studies comparing different ethnic groups. Furthermore, these findings suggest that discriminant analysis may be useful in predicting alcohol exposure in either mouse substrains.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20570474

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PubMed, Behav Brain Res. 2010 Dec 6;214(1):66-74. Epub 2010 Jun 4.

82) PATTERNS OF SOCIAL-EXPERIENCE-RELATED C-FOS AND ARC EXPRESSION IN THE FRONTAL CORTICES OF RATS EXPOSED TO SACCHARIN OR MODERATE LEVELS OF ETHANOL DURING PRENATAL BRAIN DEVELOPMENT

Hamilton DA, Candelaria-Cook FT, Akers KG, Rice JP, Maes LI, Rosenberg M, Valenzuela CF, Savage DD.
Department of Psychology, The University of New Mexico, Albuquerque, NM, USA.

ABSTRACT
Recent findings from our laboratory indicate that alterations in frontal cortex function, structural plasticity, and related social behaviors are persistent consequences of exposure to moderate levels of ethanol during prenatal brain development [24]. Fetal-ethanol-related reductions in the expression of the immediate early genes (IEGs) c-fos and Arc and alterations in dendritic spine density in ventrolateral and medial aspects of frontal cortex suggest a dissociation reminiscent of that described by Kolb et al. [38] in which these aspects of frontal cortex undergo reciprocal experience-dependent changes. In addition to providing a brief review of the available data on social behavior and frontal cortex function in fetal-ethanol-exposed rats, the present paper presents novel data on social-experience-related IEG expression in four regions of frontal cortex (Zilles LO, VLO, Fr1, Fr2) that are evaluated alongside our prior data from AID and Cg3. Social experience in normal rats was related to a distinct pattern of IEG expression in ventrolateral and medial aspects of frontal cortex, with generally greater expression observed in ventrolateral frontal cortex. In contrast, weaker expression was observed in all aspects of frontal cortex in ethanol-exposed rats, with the exception of an experience-related increase in the medial agranular cortex. Behaviors related to social investigation and wrestling/boxing were differentially correlated with patterns of activity-related IEG expression in the regions under investigation for saccharin- and ethanol-exposed rats. These observations suggest that recruitment and expression of IEGs in frontal cortex following social experience are potentially important for understanding the long-term consequences of moderate prenatal ethanol exposure on frontal cortex function, synaptic plasticity, and related behaviors.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20570698

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PubMed, Exp Toxicol Pathol. 2010 Jun 3. [Epub ahead of print]

83) ETHANOL-INDUCED INHIBITION OF FETAL HYPOTHALAMIC-PITUITARY-ADRENAL AXIS DUE TO PRENATAL OVEREXPOSURE TO MATERNAL GLUCOCORTICOID IN MICE

Liang G, Chen M, Pan XL, Zheng J, Wang H.
Pharmacology Department of Basic Medical College, Wuhan University, Wuhan 430071, China.

ABSTRACT

Prenatal ethanol exposure has been well documented to be one of the etiological factors responsible for intrauterine growth retardation (IUGR). Previous studies have shown that chronic ethanol exposure during pregnancy elevated the basic level of corticosterone in fetus. However, the potential mechanisms behind them are still unclear. The aim of the present study was to investigate the effects of prenatal ethanol exposure on maternal and fetal hypothalamic-pituitary-adrenal (HPA) axis as well as placental 11beta-hydroxysteroid dehydrogenase type 2 (11beta-HSD-2), and to clarify the mechanism of ethanol-induced IUGR. Pregnant mice were intragastricly administrated with ethanol at a dose of 6.4gkg(-1)d(-1) from day 11 to 17 of gestation and parameters representing fetal growth and development were recorded either.

The level of corticosterone in maternal serum was determined by ELISA kit. The mRNA expressions of steroidogenic acute regulatory protein (StAR) and cytochrome P450 cholesterol side chain cleavage (P450scc) both in maternal and fetal adrenal, and placental 11beta-HSD-2 were detected by real-time quantitative PCR, respectively. The results showed that fetal body weight significantly decreased, and the incidence of IUGR was obviously increased after prenatal ethanol exposure. Maternal serum corticosterone level was elevated, and the expressions of StAR and P450scc were increased in maternal adrenal while decreased in fetal adrenal. The expression of placental 11beta-HSD-2 was significantly reduced. These results suggest that prenatal ethanol exposure induces an inhibition of fetal HPA axis activity and IUGR occurs. The mechanism may be associated with ethanol-induced maternal HPA axis activation and high glucocorticoid condition, which impair the placental barrier, and lead to an overexposure of elevated maternal glucocorticoid to fetus, and eventually result in the inhibition of the fetal HPA axis.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20627497

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Nippon Koshu Eisei Zasshi. 2010 Jun;57(6):431-8.

84) EDUCATIONAL EFFECTS OF A SINGLE DISTRIBUTION OF A LEAFLET ON ALCOHOL AND PREGNANCY AMONG FEMALE UNIVERSITY STUDENTS

Mimura A, Sudo N, Kato N.
Nutrition Section, Imperial Gift Foundation, Boshi-Aiiku-Kai Aiiku Hospital.

ABSTRACT

Objective: To evaluate the educational effects of a single leaflet distributed once without explanation of its content.

Methods: All the 58 seniors on a dietitian course and all the 81 students who took "health and nutrition" as their elective in a women's university in F Prefecture were recruited. They were assigned to intervention or control groups. Both groups were asked the following choice questions in a baseline survey: "What do you think about alcohol drinking during pregnancy?" "What do you suppose you yourself will do in the future?" and "Do you know about the fetal alcohol syndrome (FAS)?" One month later, a leaflet was distributed to the intervention group only. One week after the distribution, a second

questionnaire was administered to both groups. The leaflet and the two questionnaires were distributed and collected during class with the help of teaching staff. The leaflet was made by a NPO and it recommended stopping drinking when planning to become pregnant.

Results: The participation rate was 83%. There were no significant associations between groups and grades, current drinking habit, and learning experience on this topic. Almost 80% of the intervention group read the leaflet. Change in their thinking about drinking during pregnancy before and after the intervention did not significantly differ between the two groups. Compared to 57 controls, 66 students who received the leaflet showed significant improved changes in their attitudes toward drinking during pregnancy and the knowledge about FAS.

Conclusions: No significant change in their thinking about drinking during pregnancy could be due to the fact that, even before the intervention, nearly 80% of the students thought pregnant women must abstain from alcohol entirely. This might be related to the sample characteristics, since 75% of them were majoring in nutrition. The improvement in attitudes was considered to reflect the content of the leaflet. In the intervention group, the percentage of the students who chose the alternative of "I plan to stop drinking when I wish to get pregnant" increased as the leaflet recommended and more than half of them said they learned about FAS by this leaflet. To sum up, even a single distribution of a leaflet in a school setting had educational effects which improved attitude and knowledge. Since the current sample seemed to have particular knowledge and interest in health, it is now necessary to examine effects of the same approach in the general population.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20718200

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PubMed, Behav Neurosci. 2010 Jun;124(3):362-9.

85) PRENATAL BINGE ETHANOL EXPOSURE ON GESTATION DAYS 19-20, BUT NOT ON DAYS 17-18, INCREASES POSTNATAL ETHANOL ACCEPTANCE IN RATS

Díaz-Cenzano E, Chotro MG.
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ABSTRACT

Previous research shows that prenatal binge ethanol exposure during gestation days (GD) 17 to 20 of the rat, increases postnatal ethanol intake and enhances ethanol's palatability, both effects being mediated by the opioid system. The amniotic fluid of the last period of gestation (GD 20) of the rat has been found to activate the opioid system and to induce conditioned preference in fetal and neonatal rats. We aimed to investigate whether enhanced acceptance for ethanol is observed when rat fetuses are exposed to it either on GD 17-18 or on GD 19-20. The results show that 14-day old pups whose mothers received ethanol on GD 19-20 consumed more ethanol and found ethanol more palatable when compared to pups exposed to ethanol on GD 17-18, or to pups experiencing ethanol and naloxone on GD 19-20.
The augmented ethanol intake was observed as well after weaning (PD 26-27). These data indicate that exposure to ethanol on GD 19-20, but not before, triggers appetitive learning related to ethanol's flavor. This prenatally acquired memory is retained for at least 4 weeks and can be detected postnatally as enhanced palatability of ethanol's flavor as well as increased intake of ethanol. This increased liking of ethanol is mediated by the opioid system, although it cannot be clearly determined

whether the prenatal activation of the opioid system is induced by the action of ethanol or by the activity of amniotic fluid components at that gestational age.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20528080

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Therapeutic Drug Monitoring, June 2010

86) UNIVERSAL SCREENING FOR PRENATAL ALCOHOL EXPOSURE: A PROGRESS REPORT OF A PILOT STUDY IN THE REGION OF GREY BRUCE, ONTARIO

Zelner I, Shor S, Gareri J, Lynn H, Roukema H, Lum L, Eisinga K, Nulman I, Koren G.
Division of Clinical Pharmacology & Toxicology, The Hospital for Sick Children, Toronto, Ontario.

ABSTRACT
The main objective of this study is to evaluate the clinical utility of meconium analysis for fatty acid ethyl esters as a universal screening tool intended for the detection of newborns at risk for fetal alcohol spectrum disorder. This will be accomplished by assessing the rate of voluntary participation in a nonanonymous neonatal screening program and by determining the logistics of implementing the necessary follow-up and interventions as part of routine care. Additionally, this study will determine the predictive value of fatty acid ethyl ester-positive meconium with regard to neurodevelopmental delays. This is an ongoing prospective cohort study. Written informed consent is sought from all Grey Bruce women delivering at participating birthing sites. Collected meconium samples are tested for fatty acid ethyl esters by headspace-solid-phase microextraction followed by gas chromatography-mass spectrometry. Children with positive results are followed up through an existing public health program involving regular home visits and assessments of developmental milestones by a public health nurse. These children and matched control subjects also undergo neurodevelopmental testing at 3 and 18 months of age by a clinical psychologist using Bayley Scales of Infant and Toddler Development. If delays are detected, the child is referred to diagnostic services and appropriate intervention programs. This study has been granted ethics approval and enrollment began in November 2008 at St. Joseph's Health Care in London, Ontario. The first positive case has been identified and the follow-up is currently being conducted by the public health unit. The successful completing of this study will reveal the population's willingness to participate in a neonatal screening program for prenatal alcohol exposure and determine the costs, feasibility, and utility of implementing such programs in clinical practice.

Link to the Article,
http://journals.lww.com/drug-monitoring/Abstract/2010/06000/Universal_Screening_for_Prenatal_Alcohol_Exposure_.14.aspx

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Therapeutic Drug Monitoring, June 2010

87) THE INCIDENCE OF PRENATAL ALCOHOL EXPOSURE IN MONTEVIDEO URUGUAY AS DETERMINED BY MECONIUM ANALYSIS

Hutson JR, Magri R, Gareri JN, Koren G.
Division of Clinical Pharmacology/Toxicology, Hospital for Sick Children, Toronto, Ontario, Canada.

ABSTRACT
Prenatal alcohol exposure can lead to a wide range of deficits known as fetal alcohol spectrum disorder. Epidemiologic studies regarding alcohol consumption in pregnancy have concentrated on

North America, but recent reports have suggested that consumption is significant in many parts of the world. In Uruguay, alcohol consumption has changed into more risky and dangerous patterns and thus has a theoretical risk of having a high rate of prenatal alcohol exposure. This study characterizes the incidence of prenatal alcohol exposure in Montevideo, Uruguay, using a novel biomarker, fatty acid ethyl esters, in meconium as well as a survey to mothers. Nine hundred five meconium samples were collected from Hospital Pereira Rossell and Hospital de Clínicas in Montevideo, Uruguay. A maternal questionnaire was also completed. Meconium was analyzed for fatty acid ethyl esters using liquid-liquid and solid phase extraction with gas chromatography-flame ionization detection. Meconium was also analyzed for other drugs of abuse using enzyme-linked immunosorbent assay. Forty-four percent of meconium samples were above the positive cutoff for fatty acid ethyl esters and represent those newborns with risky prenatal exposure during the final two trimesters of pregnancy. Infants with prenatal alcohol exposure were more likely to have prenatal exposure to tobacco (odds ratio, 1.56; 95% confidence interval, 1.11-2.20) or any illicit drug (odds ratio, 2.29; 95% confidence interval, 0.98-5.31). Ethyl linoleate was a significant predictor of infant birth weight along with prenatal tobacco exposure, maternal body mass index, and infant sex. This study highlights a 44% incidence of prenatal alcohol exposure.

Read Full Article,
http://journals.lww.com/drug-monitoring/Abstract/2010/06000/The_Incidence_of_Prenatal_Alcohol_Exposure_in.15.aspx

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PubMed, Yao Xue Xue Bao. 2010 Jun;45(6):705-10.

88) STEREOLOGICAL STUDY ON THE SYNAPSE LOSS IN VISUAL CORTEX OF MOUSE AFTER PRENATAL ALCOHOL EXPOSURE

Xi Y, Zhang JS, Zang JF, Wen SG, Deng JB.
Institute of Neurobiology, Henan University, Kaifeng 475004, China.

ABSTRACT

In order to understand the alcohol's toxicity to the quantitative alternations of synapses in mouse visual cortex, the expression of synaptophysin after prenatal alcohol exposure was investigated. In present study, the experimental mice at P0, P7, P14 and P30 were grouped, as control, 2 g x kg(-1) alcohol treatment and 4 g x kg(-1) alcohol treatment. The pre-synaptic elements which were used to represent synapses were marked with synaptophysin (a synaptic vesicle associated protein) by immunocytochemistry technique. The synaptophysin positive boutons in layer VI of visual cortex were imaged under laser confocal microscope. With stereological methods, the number cal density of synapse in visual cortex was calculated in different groups at various ages. Moreover, Western blotting was carried out to detect the expression of synaptophysin in visual cortex. The results showed that prenatal alcohol exposure could cause synaptic loss with long-term effect and in a dose dependent manner. For instance, there were significant difference among the different treatment groups of P0, P14 and P30 as well ($P < 0.05$). Western blotting supported the results of immunofluorescent labeling. In conclusion, prenatal alcohol exposure can induce the synaptic loss dose dependently and with long-term effect. Our findings implicate that the synaptic loss with long-term effect in CNS probably contributes to the lifelong mental retardation and memorial lowliness associated with childhood FAS.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20939177

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PubMed, BJOG. 2010 Aug;117(9):1139-50. Epub 2010 May 28.

89) LOW-MODERATE PRENATAL ALCOHOL EXPOSURE AND RISK TO CHILD BEHAVIOURAL DEVELOPMENT: A PROSPECTIVE COHORT STUDY

Robinson M, Oddy WH, McLean NJ, Jacoby P, Pennell CE, de Klerk NH, Zubrick SR, Stanley FJ, Newnham JP.
Telethon Institute for Child Health Research, Centre for Child Health Research, Perth, Australia.

ABSTRACT

Objective: To examine the association of fetal alcohol exposure during pregnancy with child and adolescent behavioural development.

Design: The Western Australian Pregnancy Cohort (Raine) Study recruited 2900 pregnancies (1989-91) and the 14-year follow up was conducted between 2003 and 2006.

Setting: Tertiary obstetric hospital in Perth, Western Australia.

Population: The women in the study provided data at 18 and 34 weeks of gestation on weekly alcohol intake: no drinking, occasional drinking (up to one standard drink per week), light drinking (2-6 standard drinks per week), moderate drinking (7-10 standard drinks per week), and heavy drinking (11 or more standard drinks per week). Methods Longitudinal regression models were used to analyse the effect of prenatal alcohol exposure on Child Behaviour Checklist (CBCL) scores over 14 years, assessed by continuous z-scores and clinical cutoff points, after adjusting for confounders.

Main Outcome Measure: Their children were followed up at ages 2, 5, 8, 10 and 14 years. The CBCL was used to measure child behaviour.

Results: Light drinking and moderate drinking in the first 3 months of pregnancy were associated with child CBCL z-scores indicative of positive behaviour over 14 years after adjusting for maternal and sociodemographic characteristics. These changes in z-score indicated a clinically meaningful reduction in total, internalising and externalising behavioural problems across the 14 years of follow up.

Conclusions: Our findings do not implicate light-moderate consumption of alcohol in pregnancy as a risk factor in the epidemiology of child behavioural problems.

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Nature, Citation: Cell Death and Disease (2010) 1, e46; doi:10.1038/cddis.2010.22
Published online 27 May 2010

90) PRENATAL ALCOHOL EXPOSURE TRIGGERS CERAMIDE-INDUCED APOPTOSIS IN NEURAL CREST-DERIVED TISSUES CONCURRENT WITH DEFECTIVE CRANIAL DEVELOPMENT

Edited by V De Laurenzi
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ABSTRACT

Fetal alcohol syndrome (FAS) is caused by maternal alcohol consumption during pregnancy. The reason why specific embryonic tissues are sensitive toward ethanol is not understood. We found that

in neural crest-derived cell (NCC) cultures from the first branchial arch of E10 mouse embryos, incubation with ethanol increases the number of apoptotic cells by fivefold. Apoptotic cells stain intensely for ceramide, suggesting that ceramide-induced apoptosis mediates ethanol damage to NCCs. Apoptosis is reduced by incubation with CDP-choline (citicoline), a precursor for the conversion of ceramide to sphingomyelin. Consistent with NCC cultures, ethanol intubation of pregnant mice results in ceramide elevation and increased apoptosis of NCCs in vivo. Ethanol also increases the protein level of prostate apoptosis response 4 (PAR-4), a sensitizer to ceramide-induced apoptosis. Prenatal ethanol exposure is concurrent with malformation of parietal bones in 20% of embryos at day E18. Meninges, a tissue complex derived from NCCs, is disrupted and generates reduced levels of TGF-β1, a growth factor critical for bone and brain development. Ethanol-induced apoptosis of NCCs leading to defects in the meninges may explain the simultaneous presence of cranial bone malformation and cognitive retardation in FAS. In addition, our data suggest that treatment with CDP-choline may alleviate the tissue damage caused by alcohol.

Read Full Article,
http://www.nature.com/cddis/journal/v1/n5/abs/cddis201022a.html

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PubMed, Neurobiol Dis. 2010 Oct;40(1):200-6. Epub 2010 May 23.

91) ALCOHOL-INDUCED NEUROAPOPTOSIS IN THE FETAL MACAQUE BRAIN

Farber NB, Creeley CE, Olney JW.
Department of Psychiatry, Washington University, St. Louis, MO 63110-1093, USA.

ABSTRACT
The ability of brief exposure to alcohol to cause widespread neuroapoptosis in the developing rodent brain and subsequent long-term neurocognitive deficits has been proposed as a mechanism underlying the neurobehavioral deficits seen in fetal alcohol spectrum disorder (FASD). It is unknown whether brief exposure to alcohol causes apoptosis in the fetal primate brain. Pregnant fascicularis macaques at various stages of gestation (G105 to G155) were exposed to alcohol for 8h, then the fetuses were delivered by caesarean section and their brains perfused with fixative and evaluated for apoptosis. Compared to saline control brains, the ethanol-exposed brains displayed a pattern of neuroapoptosis that was widespread and similar to that caused by alcohol in infant rodent brain. The observed increase in apoptosis was on the order of 60-fold. We propose that the apoptogenic action of alcohol could explain many of the neuropathological changes and long-term neuropsychiatric disturbances associated with human FASD.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20580929

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PubMed, Alcohol Alcohol. 2010 Jul-Aug;45(4):356-60. Epub 2010 May 23.

92) COMPARING THE EFFECTIVENESS OF TWEAK AND T-ACE IN DETERMINING PROBLEM DRINKERS IN PREGNANCY

Sarkar M, Einarson T, Koren G.
Division of Clinical Pharmacology and Fetal Toxicology, Hospital for Sick Children, Toronto, Canada.

ABSTRACT
Aim: The TWEAK and T-ACE screening tools are validated methods of identifying problem drinking in a pregnant population. The objective of this study was to compare the effectiveness of the TWEAK and T-ACE screening tools in identifying problem drinking using traditional cut-points (CP).

Methods: Study participants consisted of women calling the Motherisk Alcohol Helpline for information regarding their alcohol use in pregnancy. In this cohort, concerns surrounding underreporting are not likely as women self-report their alcohol consumption. Participant's self-identification, confirmed by her amount of alcohol use, determined whether she was a problem drinker or not. The TWEAK and T-ACE tools were administered on both groups and subsequent analysis was done to determine if one tool was more effective in predicting problem drinking.

Results: The study consisted of 75 problem and 100 non-problem drinkers. Using traditional CP, the TWEAK and T-ACE tools both performed similarly at identifying potential at-risk women (positive predictive value = 0.54), with very high sensitivity rates (100-99% and 100-93%, respectively) but poor specificity rates (36-43% and 19-34%, respectively). Upon comparison, there was no statistical difference in the effectiveness for one test performing better than next using either CP of 2 (P = 0.66) or CP of 3 (P = 0.38).

Conclusion: Despite the lack of difference in performance, improved specificity associated with TWEAK suggests that it may be better suited to screen at-risk populations seeking advice from a helpline.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20497951

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PubMed, Stem Cells Dev. 2010 Oct 18. Online Ahead of Print: October 18, 2010, Online Ahead of Editing: May 21, 2010

93) NEURAL DIFFERENTIATION FROM HUMAN EMBRYONIC STEM CELLS AS A TOOL TO STUDY EARLY BRAIN DEVELOPMENT AND THE NEUROTERATOGENIC EFFECTS OF ETHANOL

Taléns-Visconti R, Sanchez-Vera I, Kostic J, Perez-Arago MA, Erceg S, Stojkovic M, Guerri C.
Cell Pathology Laboratory, Centro de Investigación Príncipe Felipe , Valencia, Spain

ABSTRACT
The in vitro generation of neural cells from human embryonic stem cells is a powerful tool to acquire better knowledge of the cellular and molecular events involved in early human neural and brain development under physiological and pathological conditions. Prenatal alcohol exposure can induce important anomalies in the developing brain, the embryogenesis being an important critical period for the craniofacial defects and mental disabilities associated with fetal alcohol syndrome. Here, we report the generation of neural progenitors (NPs) from human embryonic stem cells. Neuroepithelial progenitors display the morphological and functional characteristics of their embryonic counterparts and the proper timing of neurons and glia cells generation. Immunocytochemical and real time (RT)-polymerase chain reaction analyses reveal that cells appeared as clusters during neuroepithelial cell proliferation and that the genes associated with the neuroectodermal (Pax-6) and the endodermic (α-fetoprotein) lineages decreased in parallel to the upregulation of the genes of NPs (nestin and Tuj1), followed by their differentiation into neurons (MAP-2+, GABA+), oligodendrocytes [galactocerebroside (GalC+)], and astrocytes (GFAP+). We further demonstrate, for the first time, that human NPs express the endocannabinoid receptors (CB1 and CB2) and the enzymes involved in endocannabinoids synthesis (NAPE-PLD) and degradation (FAAH). Using this in vitro culture, we demonstrate that ethanol exposure impairs NPs survival, affects the differentiation of NPs into neurons and astrocytes, disrupts the actin cytoskeleton, and affects the expression of different genes associated with neural differentiation. The results provide new insights into the effects of ethanol on human embryogenesis

and neuroprogenitors and offer an opportunity to delineate potential therapeutic strategies to restore early ethanol-induced brain damage.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20491543

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PubMed, Alcohol. 2010 May;44(3):283-90. Epub 2010 May 20.

94) REPEATED THIRD TRIMESTER-EQUIVALENT ETHANOL EXPOSURE INHIBITS LONG-TERM POTENTIATION IN THE HIPPOCAMPAL CA1 REGION OF NEONATAL RATS

Puglia MP, Valenzuela CF.
Department of Neurosciences, University of New Mexico Health Sciences Center, Albuquerque, 87131, USA.

ABSTRACT
Developmental ethanol exposure damages the hippocampus, causing long-lasting learning and memory deficits. Synaptic plasticity mechanisms (e.g., long-term potentiation [LTP]) contribute to synapse formation and refinement during development. We recently showed that acute ethanol exposure inhibits glutamatergic synaptic transmission and N-methyl-d-aspartate receptor (NMDAR)-dependent LTP in the CA1 hippocampal region of postnatal day (P)7-9 rats. The objective of this study was to further characterize the effect of ethanol on LTP in the developing CA1 hippocampus during the third trimester equivalent. To more closely model human ethanol exposure during this period, rat pups were exposed to ethanol vapor (2 or 4.5 g/dL in air, serum ethanol concentrations=96.6-147.2 or 322-395.6 mg/dL) from P2-9 (4h/d). Brain slices were prepared immediately after the end of the 4-h exposure on P7-9 and extracellular electrophysiological recordings were performed 1-7h later under ethanol-free conditions to model early withdrawal. LTP was not different than group-matched controls in the 96.6-147.2mg/dL group; however, it was impaired in the 322-395.6 mg/dL group. Neither alpha-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate receptor (AMPAR)/NMDAR function nor glutamate release were affected in the 322-395.6 mg/dL ethanol exposure group. These data suggest that repeated in vivo exposure to elevated ethanol doses during the third trimester-equivalent period impairs synaptic plasticity, which may alter maturation of hippocampal circuits and ultimately contribute to the long-lasting cognitive deficits associated with fetal alcohol spectrum disorders.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20488644

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PubMed, Brain Res Rev. 2010 Sep 24;64(2):283-303. Epub 2010 May 13.

95) HIPPOCAMPAL CELL LOSS AND NEUROGENESIS AFTER FETAL ALCOHOL EXPOSURE: INSIGHTS FROM DIFFERENT RODENT MODELS

Gil-Mohapel J, Boehme F, Kainer L, Christie BR.
Division of Medical Sciences and Department of Biology, University of Victoria, Victoria, B.C., Canada.

ABSTRACT
Prenatal ethanol exposure is invariably detrimental to the developing central nervous system and the hippocampus is particularly sensitive to the teratogenic effects of ethanol. Prenatal ethanol exposure has been shown to result in hippocampal cell loss, altered neuronal morphology and impaired

performance on hippocampal-dependent learning and memory tasks in rodents. The dentate gyrus (DG) of the hippocampus is one of the few brain regions where neurogenesis continues into adulthood. This process appears to have functional significance and these newly generated neurons are believed to play important functions in learning and memory. Recently, several groups have shown that adult hippocampal neurogenesis is compromised in animal models of fetal alcohol spectrum disorders (FASD).
The direction and magnitude of any changes in neurogenesis, however, appear to depend on a variety of factors that include: the rodent model used; the blood alcohol concentration achieved; the developmental time point when alcohol was administered; and the frequency of ethanol exposure. In this review we will provide an overview of the different rodent models of FASD that are commonly used in this research, emphasizing each of their strengths and limitations. We will also present an up-to-date summary on the effects of prenatal/neonatal ethanol exposure on adult hippocampal neurogenesis and cell loss, highlighting some of the possible molecular mechanisms that might be involved.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20471420

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PubMed, J Neurosci. 2010 May 12;30(19):6776-81.

96) LOW CONCENTRATIONS OF ALCOHOL INHIBIT BDNF-DEPENDENT GABAERGIC PLASTICITY VIA L-TYPE CA2+ CHANNEL INHIBITION IN DEVELOPING CA3 HIPPOCAMPAL PYRAMIDAL NEURONS

Zucca S, Valenzuela CF.
Department of Neurosciences, School of Medicine, University of New Mexico Health Sciences Center, Albuquerque, New Mexico 87131-0001, USA.

ABSTRACT
Fetal alcohol spectrum disorder (FASD) is associated with learning and memory alterations that could be, in part, a consequence of hippocampal damage. The CA3 hippocampal subfield is one of the regions affected by ethanol (EtOH), including exposure during the third trimester-equivalent (i.e., neonatal period in rats).
However, the mechanism of action of EtOH is poorly understood. In CA3 pyramidal neurons from neonatal rats, dendritic BDNF release causes long-term potentiation of the frequency of GABAA receptor-mediated spontaneous postsynaptic currents (LTP-GABAA) and this mechanism is thought to play a role in GABAergic synapse maturation. Here, we show that short- and long-term exposure of neonatal male rats to low EtOH concentrations abolishes LTP-GABAA by inhibiting L-type voltage-gated Ca2+ channels. These findings support the recommendation that even light drinking should be avoided during pregnancy.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20463239

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PubMed, Reprod Toxicol. 2010 Nov;30(3):489-92. Epub 2010 May 11.

97) LOW ETHANOL CONCENTRATION ALTERS CHRNA5 RNA LEVELS DURING EARLY HUMAN DEVELOPMENT

Krishnamoorthy M, Gerwe BA, Scharer CD, Heimburg-Molinaro J, Gregory F, Nash RJ, Arumugham J, Stewart B, Stice SL, Nash RJ.
Department of Anesthesiology, Emory University School of Medicine, Atlanta, GA 30322, USA.

ABSTRACT
Alcohol use is common and consumption during pregnancy has been shown to lead to a myriad of physical and neurologic abnormalities commonly referred to as fetal alcohol spectrum disorder. Substance addiction, which includes alcohol, has been shown to involve the major nicotinic acetylcholine receptor subunit CHRNA5. Using human embryonic stem cells as a model of early human development, we show that low concentrations of ethanol (20mM) can alter the expression of CHRNA5. Changes in CHRNA5 expression is linked to altered GABA and NMDA receptor expression, as well as abnormal development of the frontal cortex. These results suggest that alcohol exposure can alter early neurologic development, which may favor addiction and other developmental abnormalities in unborn children.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20438829

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PubMed, Am J Obstet Gynecol. 2010 Jul;203(1):75.e7-75.e15. Epub 2010 May 10.

98) FETAL ALCOHOL SYNDROME: CARDIAC BIRTH DEFECTS IN MICE AND PREVENTION WITH FOLATE

Serrano M, Han M, Brinez P, Linask KK.
Pediatric Residency Program, College of Medicine, University of Florida, Jacksonville, FL, USA.

ABSTRACT
Objective: Alcohol (ethanol) consumption during pregnancy is linked to congenital heart defects that are associated with fetal alcohol syndrome. Recent reports have associated ethanol exposure with the Wnt/beta-catenin pathway. Therefore, we defined whether ethanol affects Wnt/beta-catenin signaling during cardiac cell specification.

Study Design: Pregnant mice on embryonic day 6.75 during gastrulation were exposed by an intraperitoneal injection to a binge-drinking dose of ethanol. Folic acid supplementation of mouse diet was tested for the prevention of ethanol-induced cardiac birth defects.

Results: Acute ethanol exposure induced myocardial wall changes and atrioventricular and semilunar valve defects, which was determined by echocardiography on embryonic day 15.5. A high folate diet prevented the ethanol-induced cardiac defects. Ethanol exposure in avian embryos suppressed 2 key Wnt-modulated genes that are involved in cardiac induction; folic acid rescued normal gene expression.

Conclusion: Folic acid supplementation alone or with myoinositol prevented alcohol potentiation of Wnt/beta-catenin signaling that allowed normal gene activation and cardiogenesis.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20451895

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PubMed, Physiol Behav. 2010 Aug 4;101(1):153-60. Epub 2010 May 6.

99) PARTICIPATION OF THE ENDOGENOUS OPIOID SYSTEM IN THE ACQUISITION OF A PRENATAL ETHANOL-RELATED MEMORY: EFFECTS ON NEONATAL AND PREWEANLING RESPONSIVENESS TO ETHANOL

Miranda-Morales RS, Molina JC, Spear NE, Abate P.
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ABSTRACT
The present study tested the involvement of the opioid system in the acquisition and expression of prenatal ethanol-related memories. We evaluated how this prenatal experience modulates ethanol self-administration in newborn rats, and preweanling's ingestion of the drug. During Gestational Days (GDs) 17-20, four groups of dams were treated with ethanol (2 g/kg) or water, followed immediately by naloxone (10 mg/kg) or saline administration. A fifth group received a similar dose of naloxone 20min before ethanol administration. On PD 1, pups were tested on an operant learning procedure to obtain milk or 3% ethanol. One hour later, an extinction session was performed. At Postnatal Days (PDs) 14 and 15, preweanlings representing each prenatal treatment were evaluated in an intake test with infusions of 5% ethanol or water. Prior to the intake test on PD14, preweanlings were administered naloxone (1 mg/kg), saline or remained untreated. In both tests, animals representative of both genders were utilized. One-day-old pups rapidly learned the operant behavior to gain access to milk. In contrast, only pups prenatally treated with ethanol (administered immediately before naloxone or saline injection) increased operant responding to gain access to ethanol. On an intake test at PDs 14 and 15, those animals prenatally exposed to naloxone 20 min before ethanol administration consumed significantly lower ethanol levels than the remaining prenatal ethanol groups. Postnatal treatment with naloxone diminished intake of all solutions at PD14. These results suggest that prenatal ethanol exposure facilitates neonatal operant learning reinforced by intraoral administration of ethanol and increases ethanol consumption during PDs 14-15. The endogenous opioid system apparently is involved in the acquisition of prenatal ethanol memories, which can modulate the reinforcing attributes of the drug in neonatal and preweanling rats.

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http://www.ncbi.nlm.nih.gov/pubmed/20451537

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PubMed, Am J Perinatol. 2010 Oct;27(9):743-8. Epub 2010 May 4.

100) TREATMENT WITH NEUROPEPTIDES ATTENUATES C-FOS EXPRESSION IN A MOUSE MODEL OF FETAL ALCOHOL SYNDROME

Incerti M, Vink J, Roberson R, Abebe D, Spong CY.
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ABSTRACT
Fetal alcohol syndrome (FAS) is the most common nongenetic cause of mental retardation and is characterized by neurodevelopmental anomalies. C-FOS is a cellular marker of transcriptional activity in the stress-signal pathway. Previously, we showed the treatment with NAP (NAPVSIPQ) + SAL (SALLRSIPA) reversed the learning deficit after prenatal alcohol exposure in FAS. Our objective was to evaluate if the mechanism of actions of NAP + SAL involves the stress-signal pathway differentiating C-FOS expression in mouse brains after prenatal alcohol exposure. C57Bl6/J mice were treated with alcohol (0.03 mL/g) or placebo on gestational day 8. On postnatal day 40, in utero

alcohol-exposed males were treated via gavage with 40 µg D-NAP and 40 µg D-SAL (N = 6) or placebo (N = 4); controls were gavaged with placebo daily (N = 12). After learning evaluation, hippocampus, cerebellum, and cortex were isolated. Calibrator-normalized relative real-time polymerase chain reaction and Western blot analysis were performed. Statistics included analysis of variance and post hoc Fisher analysis. Adult treatment with NAP + SAL restored the down-regulation of C-FOS in the hippocampus after prenatal alcohol exposure (P < 0.05), but not in the cerebellum. There was no difference in C-FOS expression in the cortex. Adult treatment with NAP + SAL restored the down-regulation of C-FOS expression in hippocampus attenuating the alcohol-induced alteration of the stress-signal pathway.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20446212

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PubMed, Matern Child Health J. 2010 May 1. [Epub ahead of print]

101) ALCOHOL CONSUMPTION DURING PREGNANCY AND RISK OF PLACENTAL ABRUPTION AND PLACENTA PREVIA

Aliyu MH, Lynch O, Nana PN, Alio AP, Wilson RE, Marty PJ, Zoorob R, Salihu HM.
Department of Preventive Medicine, Institute for Global Health, Vanderbilt University, Nashville, TN, USA.

ABSTRACT
The purpose of this study was to examine the association between prenatal alcohol consumption and the occurrence of placental abruption and placenta previa in a population-based sample. We used linked birth data files to conduct a retrospective cohort study of singleton deliveries in the state of Missouri during the period 1989 through 2005 (n = 1,221,310). The main outcomes of interest were placenta previa, placental abruption and a composite outcome defined as the occurrence of either or both lesions. Multivariate logistic regression was used to generate adjusted odd ratios, with non-drinking mothers as the referent category. Women who consumed alcohol during pregnancy had a 33% greater likelihood for placental abruption during pregnancy (adjusted odds ratio (OR), 95% confidence interval (CI) = 1.33 [1.16-1.54]). No association was observed between prenatal alcohol use and the risk of placenta previa. Alcohol consumption in pregnancy was positively related to the occurrence of either or both placental conditions (adjusted OR [95% CI] = 1.29 [1.14-1.45]). Mothers who consumed alcohol during pregnancy were at elevated risk of experiencing placental abruption, but not placenta previa. Our findings underscore the need for screening and behavioral counseling interventions to combat alcohol use by pregnant women and women of childbearing age.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20437196

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PubMed, Womens Health Issues. 2010 May-Jun;20(3):193-200.

102) WOMEN'S PERSPECTIVES ON SCREENING FOR ALCOHOL AND DRUG USE IN PRENATAL CARE

Roberts SC, Nuru-Jeter A.
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ABSTRACT
Background: Screening for alcohol and drug use in prenatal care is widely promoted in the United States as a public health strategy for reducing alcohol and drug use during pregnancy. However, the

published literature does not consider women's perspectives or the potential negative ramifications of screening.

Methods: Twenty semistructured interviews and two focus groups (n = 38) were conducted with a racially/ethnically diverse sample of low-income pregnant and parenting women using alcohol and/or drugs in a northern California county.

Results: Most women were averse to having drug but not alcohol use identified and were mistrustful of providers' often inconspicuous efforts to discover drug use. Women expected psychological, social, and legal consequences from being identified, including feelings of maternal failure, judgment by providers, and reports to Child Protective Services. Women did not trust providers to protect them from these consequences. Rather, they took steps to protect themselves. They avoided and emotionally disengaged from prenatal care, attempted to stop using substances that could be detected by urine tests before prenatal care visits, and shared strategies within social networks for gaining the benefits of prenatal care while avoiding its negative consequences.

Conclusion: Considerations of the public health impact of screening for drug use in prenatal care should account for the implications of women's physical avoidance of and emotional disengagement from prenatal care, specifically the direct effects of late, limited, and no prenatal care on pregnancy outcomes and missed opportunities for health promoting interventions.

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http://www.ncbi.nlm.nih.gov/pubmed/20457407

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PubMed, Am J Obstet Gynecol. 2010 May;202(5):457.e1-4.

103) PREVENTION OF THE ALCOHOL-INDUCED CHANGES IN BRAIN-DERIVED NEUROTROPHIC FACTOR EXPRESSION USING NEUROPROTECTIVE PEPTIDES IN A MODEL OF FETAL ALCOHOL SYNDROME

Incerti M, Vink J, Roberson R, Benassou I, Abebe D, Spong CY.
Unit on Perinatal and Developmental Neurobiology, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institute of Health, Bethesda, MD, USA.

ABSTRACT
Objective: Our objective was to evaluate whether brain-derived neurotrophic factor (BDNF) expression is affected by prenatal alcohol exposure and whether the neuroprotective effects of the vasoactive intestinal peptide (VIP)-related peptides, NAPVSIPQ (NAP) and SALLRSIPA (SAL), are mediated through BDNF.

Study Design: Using a well-characterized fetal alcohol syndrome (FAS) model, timed pregnant C57BL6/J mice were treated on gestational day (E) 8 with alcohol (0.03 mL/g), placebo, or alcohol plus (NAP plus SAL). Embryos were harvested at 6 hours (E8), 24 hours (E9), and 10 days (E18) and pups at postnatal day 40. Calibrator-normalized relative real time polymerase chain reaction was performed to quantify BDNF with hypoxanthine phosphoribosyl transferase-1 standardization.

Results: BDNF expression was lower in the alcohol-exposed embryos than in controls at 6 hours and higher at 24 hours and 10 days (all P<.05). Pretreatment with NAP plus SAL prevented the alcohol-induced rise in BDNF expression (P<.05) at 24 hours and 10 days after alcohol exposure. We found no difference between alcohol and control in young-adults' brain (P>.05).

Conclusion: NAP plus SAL treatment prevented alcohol-induced changes in BDNF expression 24 hours and 10 days after alcohol exposure in mouse embryos. This may explain, at least in part, the peptides' prevention of neurodevelopmental anomalies in FAS.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20452488

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PubMed, Cancer Epidemiol Biomarkers Prev. 2010 May;19(5):1238-60.

104) MATERNAL ALCOHOL CONSUMPTION DURING PREGNANCY AND RISK OF CHILDHOOD LEUKEMIA: SYSTEMATIC REVIEW AND META-ANALYSIS

Latino-Martel P, Chan DS, Druesne-Pecollo N, Barrandon E, Hercberg S, Norat T.
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ABSTRACT

Background: Leukemia is the most frequently occurring cancer in children. Although its etiology is largely unknown, leukemia is believed to result from an interaction between genetic and environmental factors. Among different potential risk factors, the possible role of maternal alcohol consumption during pregnancy has been questioned.

Methods: To assess the association between maternal alcohol consumption during pregnancy and childhood leukemia, a systematic review and meta-analysis of published studies was done.

Results: Twenty-one case-control studies were included in categorical and dose-response meta-analyses. No cohort study was identified. Analyses were conducted by type of leukemia, children's age at diagnosis, and type of alcoholic beverage and trimester of pregnancy at alcohol use. Alcohol intake during pregnancy (yes versus no) was statistically significantly associated with childhood acute myeloid leukemia (AML) [odds ratio (OR), 1.56; 95% confidence interval (CI), 1.13-2.15] but not with acute lymphoblastic leukemia (OR, 1.10; 95% CI, 0.93-1.29). Heterogeneity between studies was observed. The OR of AML for an increase of a drink per week was 1.24 (95% CI, 0.94-1.64). The association of alcohol intake during pregnancy with AML was observed for cancers diagnosed at age 0 to 4 years (OR, 2.68; 95% CI, 1.85-3.89) in five studies without heterogeneity (I2<or=0.1%).

Conclusions: The results of case-control studies indicate that maternal alcohol consumption during pregnancy is associated with a significantly increased risk of AML in young children.

Impact: Avoidance of maternal alcohol drinking during pregnancy might contribute to a decrease in the risk of childhood AML.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20447918

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PubMed, Arch Pediatr Adolesc Med. 2010 May;164(5):452-6.

105) SLEEP PROBLEMS IN CHILDREN WITH PRENATAL SUBSTANCE EXPOSURE: THE MATERNAL LIFESTYLE STUDY

Stone KC, LaGasse LL, Lester BM, Shankaran S, Bada HS, Bauer CR, Hammond JA.
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ABSTRACT

Objective: To examine the associations between sleep problems and prenatal exposure to cocaine, opiates, marijuana, alcohol, and nicotine in children aged 1 month to 12 years.

Design: Sleep data were collected by maternal report in a prospective longitudinal follow-up of children participating in the Maternal Lifestyle multisite study.

Setting: Hospital-based research centers in Providence, Rhode Island; Miami, Florida; Detroit, Michigan; and Memphis, Tennessee.

Participants: There were 808 participants, 374 exposed to cocaine and/or opiates, and 434 comparison subjects.

Main Exposure: Prenatal cocaine, opiate, marijuana, alcohol, and/or nicotine exposure.

Outcome Measure: Sleep problems in early, middle, and/or late childhood, assessed as composites of maternal report items.

Results: Of the 5 substances, prenatal nicotine exposure was the only unique predictor of sleep problems (B = 0.074, R(2) change = 0.008, P = .01), with adjustment for covariates, including socioeconomic status, marital status, physical abuse, prenatal medical care, and postnatal cigarette smoke exposure.

Conclusions: Prenatal exposure to nicotine was positively associated with children's sleep problems persisting throughout the first 12 years of life. Targeting of this group of children for educational and behavioral efforts to prevent and treat sleep problems is merited given that good sleep may serve as a protective factor for other developmental outcomes.

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http://www.ncbi.nlm.nih.gov/pubmed/20439796

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PubMed, Arch Pediatr Adolesc Med. 2010 May;164(5):419-24.

106) ENDURING EFFECTS OF PRENATAL AND INFANCY HOME VISITING BY NURSES ON MATERNAL LIFE COURSE AND GOVERNMENT SPENDING: FOLLOW-UP OF A RANDOMIZED TRIAL AMONG CHILDREN AT AGE 12 YEARS

Olds DL, Kitzman HJ, Cole RE, Hanks CA, Arcoleo KJ, Anson EA, Luckey DW, Knudtson MD, Henderson CR Jr, Bondy J, Stevenson AJ.
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ABSTRACT

Objective: To test, among an urban primarily African American sample, the effects of prenatal and infancy home visiting by nurses on mothers' fertility, partner relationships, and economic self-sufficiency and on government spending through age 12 years of their firstborn child.

Design: Randomized controlled trial.

Setting: Public system of obstetric and pediatric care in Memphis, Tennessee.

Participants: A total of 594 urban primarily African American economically disadvantaged mothers (among 743 who registered during pregnancy). Intervention Prenatal and infancy home visiting by nurses.

Main Outcome Measures: Mothers' cohabitation with and marriage to the child's biological father, intimate partner violence, duration (stability) of partner relationships, role impairment due to alcohol and other drug use, use and cost of welfare benefits, arrests, mastery, child foster care placements, and cumulative subsequent births.

Results: By the time the firstborn child was 12 years old, nurse-visited mothers compared with control subjects reported less role impairment owing to alcohol and other drug use (0.0% vs 2.5%, P = .04), longer partner relationships (59.58 vs 52.67 months, P = .02), and greater sense of mastery (101.04 vs 99.60, P = .005). During this 12-year period, government spent less per year on food stamps, Medicaid, and Aid to Families with Dependent Children and Temporary Assistance for Needy Families for nurse-visited than control families ($8772 vs $9797, P = .02); this represents $12 300 in discounted savings compared with a program cost of $11 511, both expressed in 2006 US dollars. No statistically significant program effects were noted on mothers' marriage, partnership with the child's biological father, intimate partner violence, alcohol and other drug use, arrests, incarceration, psychological distress, or reports of child foster care placements.

Conclusion: The program improved maternal life course and reduced government spending among children through age 12 years.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20439792

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PubMed, J Dev Behav Pediatr. 2010 May;31(4):304-16.

107) POPULATION DIFFERENCES IN DYSMORPHIC FEATURES AMONG CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS

May PA, Gossage JP, Smith M, Tabachnick BG, Robinson LK, Manning M, Cecanti M, Jones KL, Khaole N, Buckley D, Kalberg WO, Trujillo PM, Hoyme HE.
Center on Alcoholism, Substance Abuse, and Addictions (CASAA), The University of New Mexico, Albuquerque, NM 87106, USA. pmay@unm.edu;phyl@unm.edu

ABSTRACT
Objective: To examine the variation in significant dysmorphic features in children from 3 different populations with the most dysmorphic forms of fetal alcohol spectrum disorders, fetal alcohol syndrome (FAS), and partial fetal alcohol syndrome (PFAS).

Method: Advanced multiple regression techniques are used to determine the discriminating physical features in the diagnosis of FAS and PFAS among children from Northern Plains Indian communities, South Africa, and Italy.

Results: Within the range of physical features used to identify children with fetal alcohol spectrum disorders, specifically FAS and PFAS, there is some significant variation in salient diagnostic features

from one population to the next. Intraclass correlations in diagnostic features between these 3 populations is 0.20, indicating that about 20% of the variability in dysmorphology core features is associated with location and, therefore, specific racial/ethnic population. The highly significant diagnostic indicators present in each population are identified for the full samples of FAS, PFAS, and normals and also among children with FAS only. A multilevel model for these populations combined indicates that these variables predict dysmorphology unambiguously: small palpebral fissures, narrow vermillion, smooth philtrum, flat nasal bridge, and fifth finger clinodactyly. Long philtrum varies substantially as a predictor in the 3 populations. Predictors not significantly related to fetal alcohol spectrum disorders dysmorphology across the 3 populations are centile of height (except in Italy) strabismus, interpupilary distance, intercanthal distance, and heart murmurs.

Conclusion: The dysmorphology associated with FAS and PFAS vary across populations, yet a particular array of common features occurs in each population, which permits a consistent diagnosis across populations.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20431397

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PubMed, Genome Med. 2010 Apr 28;2(4):27.

108) GENETIC AND EPIGENETIC INSIGHTS INTO FETAL ALCOHOL SPECTRUM DISORDERS

Ramsay M.
Division of Human Genetics, National Health Laboratory Service and School of Pathology, University of the Witwatersrand, Johannesburg, 2000, South Africa. Michele.ramsay@nhls.ac.za.

ABSTRACT
The magnitude of the detrimental effects following in utero alcohol exposure, including fetal alcohol syndrome and other fetal alcohol spectrum disorders (FASD), is globally underestimated. The effects include irreversible cognitive and behavioral disabilities as a result of abnormal brain development, pre- and postnatal growth retardation and facial dysmorphism. Parental alcohol exposure and its effect on offspring has been recognized for centuries, but only recently have we begun to gain molecular insight into the mechanisms involved in alcohol teratogenesis. Genetic attributes (susceptibility and protective alleles) of the mother and the fetus contribute to the risk of developing FASD and specific additional environmental conditions, including malnutrition, have an important role. The severity of FASD depends on the level of alcohol exposure, the developmental stage at which exposure occurs and the nature of the exposure (chronic or acute), and although the most vulnerable period is during the first trimester, damage can occur throughout gestation. Preconception alcohol exposure can also have a detrimental effect on the offspring. Several developmental pathways are affected in FASD, including nervous system development, growth and remodeling of tissues, as well as metabolic pathways that regulate glucocorticoid signaling and balanced levels of retinol, insulin and nitric oxide. A body of knowledge has accumulated to support the role of environmentally induced epigenetic remodeling during gametogenesis and after conception as a key mechanism for the teratogenic effects of FASD that persist into adulthood. Transgenerational effects are likely to contribute to the global burden of alcohol-related disease. FASD results in lifelong disability and preventative programs should include both maternal alcohol abstention and preconception alcohol avoidance.

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Can J Clin Pharmacol Vol 17 (1) Winter 2010:e177-e193; April 15, 2010

109) A REVIEW OF SUBSTANCE ABUSE MONITORING IN A SOCIAL SERVICES CONTEXT: A PRIMER FOR CHILD PROTECTION WORKERS

Monique Moller, Joey Gareri, Gideon Koren

ABSTRACT

As drug abuse in our society escalates, child protection workers face mounting challenges in accurately assessing parental substance abuse in the interest of effective child protection. The impartial evaluation of substance use and abuse is fundamental, requiring objective and sensitive methods. A variety of biological specimens, some applicable to short-term and some to long-term monitoring, have been successful when applied to a child protection and drug abuse monitoring of caregivers. This article explores the complementary features of drug testing in urine, hair, and meconium, among other alternative matrices and discusses the practicality, basic science, and applicability of each to substance abuse monitoring in the context of child protection.

Read Full Article,
http://www.cjcp.ca/pubmed.php?articleId=260

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PubMed, Neurosci Lett. 2010 Apr 12;473(3):202-7. Epub 2010 Feb 26.

110) PHOSPHODIESTERASE TYPE 1 INHIBITION IMPROVES LEARNING IN RATS EXPOSED TO ALCOHOL DURING THE THIRD TRIMESTER EQUIVALENT OF HUMAN GESTATION

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ABSTRACT

Deficits in learning and memory have been extensively observed in animal models of fetal alcohol spectrum disorders (FASD). Here we use the Morris maze to test whether vinpocetine, a phosphodiesterase type 1 inhibitor, restores learning performance in rats exposed to alcohol during the third trimester equivalent of human gestation. Long Evans rats received ethanol (5g/kg i.p.) or saline on alternate days from postnatal day (P) 4 to P10. Two weeks later (P25), the latency to find a hidden platform was evaluated (2 trials per day spaced at 40-min inter-trial intervals) during 4 consecutive days. Vinpocetine treatment started on the first day of behavioral testing: animals received vinpocetine (20mg/kg i.p.) or vehicle solution every other day until the end of behavioral procedures. Early alcohol exposure significantly affected the performance to find the hidden platform. The average latency of ethanol-exposed animals was significantly higher than that observed for the control group. Treatment of alcohol-exposed animals with vinpocetine restored their performance to control levels. Our results show that inhibition of PDE1 improves learning and memory deficits in rats early exposed to alcohol and provide evidence for the potential therapeutic use of vinpocetine in FASD.

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Wiley Online Library – Alcoholsh: Clinical and Experimental Research. Article first published online: 5 APR 2010

111) STRUCTURAL AND FUNCTIONAL EFFECTS OF DEVELOPMENTAL EXPOSURE TO ETHANOL ON THE ZEBRAFISH HEART

Cynthia A. Dlugos, Richard A. Rabin

ABSTRACT

Background: Fetal alcohol exposure during development results in a host of cardiac abnormalities including atrial and ventricular septal defects, teratology of Fallot, d-transposition of the great arteries, truncus arteriosus communis, and aortico-pulmonary window. The mechanisms behind these ethanol-induced deficits are unknown. The purpose of this study was to determine whether the zebrafish, a simple model in which heart development and the sequence of gene expression is well elucidated and comparable to that in higher vertebrates, is sensitive to developmental exposure of pharmacologically relevant concentrations of ethanol.

Methods: Zebrafish eggs of the AB strain were raised in egg water or in 0.5% (v/v) ethanol solution for either 54 hpf (hours postfertilization) or 72 hpf. Heart pathology and volumes were evaluated on the latter group at 5 dpf (days postfertilization) on tissue sections from fixed larvae embedded in glycolmethacrylate. Heart rates were determined in embryos of 54 hpf and larvae of 5 dpf. The functional maturity of the heart's conducting system was measured by determining the response of ethanol-treated and control embryos and larvae to the adrenergic agonist, isoproterenol, and the cholinergic agonist, carbachol.

Results: Ethanol-induced alterations occurred in heart morphology and heart volume. A developmental lag in the isoproterenol response and the absence of carbachol-mediated bradycardia were also observed following ethanol treatment.

Conclusions: These results show that exposure of the zebrafish to ethanol during development results in structural and functional changes in the heart that mimic malformations that occur in patients with fetal alcohol syndrome (FAS). These findings promote the zebrafish heart as a future model for investigating the mechanisms responsible for ethanol's adverse effects on vertebrate heart development.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1111/j.1530-0277.2010.01176.x/abstract

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Wiley Online Library – Alcoholsh: Clinical and Experimental Research. Article first published online: 5 APR 2010

112) ADVANCING ALCOHOL BIOMARKERS RESEARCH

Cynthia F. Bearer, Shannon M. Bailey, Jan B. Hoek

ABSTRACT

Biomarkers to detect past alcohol use and identify alcohol-related diseases have long been pursued as important tools for research into alcohol use disorders as well as for clinical and treatment applications and other settings. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) sponsored a workshop titled "Workshop on Biomarkers for Alcohol-Induced Disorders" in June 2008. The intent of this workshop was to review and discuss recent progress in the development and implementation of biomarkers for alcohol use and alcohol-related disorders with a goal to formulate a

set of recommendations to use to stimulate and advance research progress in this critical area of alcoholism research. Presentations at this workshop reviewed the current status of alcohol biomarkers, providing a summary of the history of biomarkers and the major goals of alcohol biomarker research. Moreover, presentations provided a comprehensive overview of the current status of several well-recognized biomarkers of alcohol use, a summary of recent studies to characterize novel biomarkers and their validation, along with perspectives and experiences from other NIH institutes and from other federal agencies and industry, related to regulatory issues. Following these presentations, a panel discussion focused on a set of issues presented by the organizers of this workshop. These discussion points addressed: (i) issues related to strategies to be adopted to stimulate biomarker discovery and application, (ii) the relevance of animal studies in biomarker development and the status of biomarkers in basic science studies, and (iii) issues related to the opportunities for clinical and commercial applications. This article summarizes these perspectives and highlights topics that constituted the basis for recommendations to enhance alcohol biomarker research.

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1111/j.1530-0277.2010.01168.x/abstract

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PubMed, Neurotoxicol Teratol. 2010 Mar-Apr;32(2):164-70.

113) DIFFERENTIAL EFFECTS OF CHRONIC ETHANOL EXPOSURE ON CYTOCHROME P450 2E1 AND THE HYPOTHALAMIC-PITUITARY-ADRENAL AXIS IN THE MATERNAL-FETAL UNIT OF THE GUINEA PIG

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ABSTRACT
Background: Ethanol neurobehavioural teratogenicity is a leading cause of developmental mental deficiency, in which the hippocampus is a target site of injury. The multi-faceted mechanism of ethanol teratogenicity is not completely understood. This study tested the hypothesis that chronic ethanol exposure (CEE), via chronic maternal ethanol administration, increases cytochrome P450 2E1 (CYP2E1) expression and alters hypothalamic-pituitary-adrenal (HPA) axis activity in the maternal-fetal unit during the third-trimester-equivalent of gestation.

Methods: Pregnant Dunkin-Hartley-strain guinea pigs received daily oral administration of ethanol (4 g ethanol/kg maternal body weight) or isocaloric-sucrose/pair-feeding (control) throughout gestation (term, about gestational day (GD) 68). On GD 45, 55 and 65, pregnant animals were euthanized 2h after the last daily dose. Maternal and fetal body weights and fetal hippocampal brain weight were determined. Maternal and fetal samples were collected for the determination of liver CYP2E1 enzymatic activity and plasma free cortisol and ACTH concentrations.

Results: CEE, with maternal blood ethanol concentration of 108-124 mg/dl at 2h after the last dose, decreased fetal hippocampal weight only at GD 65 and had no effect on fetal body weight compared with control. CYP2E1 activity increased with gestational age in the fetal liver microsomal and mitochondrial fractions. CEE increased CYP2E1 activity in the microsomal and mitochondrial fractions of maternal liver at the three gestational ages and in both hepatic subcellular fractions of the GD 65 fetus compared with control. There was a gestational-age-dependent increase in maternal and fetal plasma free cortisol concentrations, but no effect of CEE compared with control. Maternal and fetal plasma ACTH concentrations were unaffected by CEE compared with control, and were virtually unchanged during the third-trimester-equivalent that was studied.

Conclusion: These data demonstrate that, in the pregnant guinea pig, this CEE regimen increases liver CYP2E1 activity, without affecting HPA axis function, in the maternal-fetal unit during near-term gestation. The CEE-induced increase in liver CYP2E1 activity and potential oxidative stress in the maternal-fetal unit may play a role in the pathogenesis of ethanol teratogenicity.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20006703

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PubMed, Psychiatry Investig. 2010 June; 7(2): 86–92. Published online 2010 April 6. doi: 10.4306/pi.2010.7.2.86.

114) ALCOHOL USE DURING PREGNANCY AND RELATED RISK FACTORS IN KOREA

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ABSTRACT

Objective: The number of Korean women of childbearing age who drink alcohol and binge drink has increased remarkably in recent years. In the present study, we examined self-reported rates of alcohol use before and during pregnancy and identified maternal characteristics associated with drinking in pregnancy.

Methods: One thousand pregnant Korean women who visited the Department of Obstetrics and Gynecology (OB/GYN) completed a self-administered questionnaire that sought information on their demographic characteristics and incorporated features of the Alcohol Use Disorder Identification Test (AUDIT)-C to investigate their use of alcohol, including binge drinking, during three time periods ("in the year before this pregnancy," "during this pregnancy," and "in the previous 30 days").

Results: Of these participants, 16.4% reported using alcohol during their pregnancy, 12.2% had used alcohol in the previous 30 days, and 1.7% reported binge drinking during their pregnancy. In the year before pregnancy, 77.1% had used alcohol, and 22.3% had binge drunk. The group using any amount of any alcohol during pregnancy showed a lower educational level, a lower rate of planned pregnancy, a lower level of knowledge relating to the risks of drinking alcohol during pregnancy, and a higher frequency of alcohol drinking in the year before pregnancy when compared with the abstinent group. Low educational level and unplanned pregnancy were revealed to be significant risk factors for alcohol consumption in pregnant women.

Conclusion: This is the first study to examine any alcohol and binge alcohol drinking during pregnancy in Korea. Clinical attention and monitoring system on alcohol use during pregnancy are necessary in Korea.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2890873/

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PubMed, Int J Environ Res Public Health. 2010 February; 7(2): 364–379. Published online 2010 January 27. doi: 10.3390/ijerph7020364.

115) ALCOHOL ABUSE IN PREGNANT WOMEN: EFFECTS ON THE FETUS AND NEWBORN, MODE OF ACTION AND MATERNAL TREATMENT

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ABSTRACT
Offspring of mothers using ethanol during pregnancy are known to suffer from developmental delays and/or a variety of behavioral changes. Ethanol, may affect the developing fetus in a dose dependent manner. With very high repetitive doses there is a 6–10% chance of the fetus developing the fetal alcoholic syndrome manifested by prenatal and postnatal growth deficiency, specific craniofacial dysmorphic features, mental retardation, behavioral changes and a variety of major anomalies. With lower repetitive doses there is a risk of “alcoholic effects” mainly manifested by slight intellectual impairment, growth disturbances and behavioral changes. Binge drinking may impose some danger of slight intellectual deficiency. It is advised to offer maternal abstinence programs prior to pregnancy, but they may also be initiated during pregnancy with accompanying close medical care. The long term intellectual outcome of children born to ethanol dependent mothers is influenced to a large extent by the environment in which the exposed child is raised.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2872283/?tool=pubmed

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Wiley Online Library – Basic and Clinical Pharmacology and Toxicology, Article first published online: 14 JAN 2010

116) A LOW ETHANOL DOSE AFFECTS ALL TYPES OF CELLS IN MIXED LONG-TERM EMBRYONIC CULTURES OF THE CEREBELLUM

Chris Pickering, Grzegorz Wicher, Sofi Rosendahl, Helgi B. Schiöth, Åsa Fex-Svenningsen

ABSTRACT
The beneficial effect of the ‘1-drink-a-day’ lifestyle is suggested by studies of cardiovascular health, and this recommendation is increasingly followed in many countries. The main objective of this study

was to determine whether this pattern of ethanol use would be detrimental to a pregnant woman. We exposed a primary culture of rat cerebellum from embryonic day 17 (corresponding to second trimester in humans) to ethanol at a concentration of 17.6 mM which is roughly equivalent to one glass of wine. Acutely, there was no change in cell viability after 5 or 8 days of exposure relative to control. By 11 days, a reduction in the number of viable cells was observed without an accompanying change in caspase-3 activity (marker of apoptotic cell death), suggesting changes in cell proliferation. As the proportion of nestin-positive cells was higher in the ethanol-treated cultures after 5 days, we hypothesized that an increase in differentiation to neurons would compensate for the ongoing neuronal death. However, there were limits to this compensatory ability as the relative proportion of nestin-positive cells was decreased after 11 days. To further illustrate the negative long-term effects of this ethanol dose, cultures were exposed for 30 days. After this period, virtually no neurons or myelinating oligodendrocytes were present in the ethanol-treated cultures. In conclusion, chronic exposure to ethanol, even at small doses, dramatically and persistently affects normal development

Read Full Article,
http://onlinelibrary.wiley.com/doi/10.1111/j.1742-7843.2009.00528.x/abstract

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PubMed, Ned Tijdschr Geneeskd. 2010;154(34):A331.

117) DIAGNOSIS OF FETAL ALCOHOL SPECTRUM DISORDERS

Van Wieringen H, Letteboer TG, Pereira RR, de Ruiter S, Balemans WA, Lindhout D.
St. Antoniusziekenhuis, afd. Kindergeneeskunde, Nieuwegein, the Netherlands.

ABSTRACT

Prenatal alcohol exposure may cause decreased growth of the child, congenital abnormalities, specific facial characteristics, and, most importantly, mental retardation and behavioural disorders, all known as fetal alcohol spectrum disorders (FASD). A significant number of pregnant women in the Netherlands drink alcohol, but the prevalence of FASD in our country is unknown. Repeated and high peak blood alcohol concentrations, for example in the case of binge drinking by the mother, result in more severe abnormalities; a safe limit for alcohol consumption in pregnancy cannot be defined. In 2007 and 2008, Dutch paediatricians reported a total of 56 diagnosed cases of FASD, mostly adopted and foster children. Possibly the condition has not always been diagnosed. Use of international guidelines for diagnosis by the medical profession may improve detection. The guidelines of the Canadian Public Health Agency provide a useful and generally accepted classification, with strict cut-off points to avoid overdiagnosis; attention should always be paid to the broad differential diagnosis.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20858301

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PubMed, Child Welfare. 2010;89(1):7-29.

118) SUPPORTING RESILIENCE IN FOSTER FAMILIES: A MODEL FOR PROGRAM DESIGN THAT SUPPORTS RECRUITMENT, RETENTION, AND SATISFACTION OF FOSTER FAMILIES WHO CARE FOR INFANTS WITH PRENATAL SUBSTANCE EXPOSURE

Marcellus L.
University of Victoria.

ABSTRACT

As the health, social, and developmental needs of infants in foster care become more complex, foster families are challenged to develop specialized knowledge to effectively address these needs. The goal

of this qualitative research study was to identify the process of becoming a foster family and providing family foster caregiving within the context of caring for infants with prenatal drug and alcohol exposure. A constructivist grounded theory approach was used to study foster families (including mothers, fathers, and birth and adoptive children) who specialized in caring for infants within a Canadian provincial child welfare system. This article describes an infant foster care model, applies resilience theory to the model, and provides recommendations for program development for foster families that specialize in the infant population.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20565011

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PubMed, Adicciones. 2010;22(2):97-9.

119) NEW INFORMATIVE AND PREVENTION PROGRAMS IN EUROPE TO REDUCE THE RISKS ASSOCIATED TO ALCOHOL CONSUMPTION DURING PREGNANCY AND THE APPEARANCE OF FOETAL ALCOHOL SPECTRUM DISORDERS

Guerri C.

ABSTRACT
In the last 40 years a vast mass of clinical, epidemiological and experimental evidence has demonstrated that alcohol is a teratogenic agent and that its consumption during gestation can cause foetal death, malformations and cognitive and behavioral dysfunctions in the exposed fetus. The most dramatic presentation is the complete foetal alcohol syndrome (FAS), which is observed in children born from heavy alcohol consuming mothers. FAS and of other fetal alcohol-related effects was reported in both USA and Europe in the middle 80 s. However, despite these evidences, many European countries have largely forgotten or minimize the risks associated with prenatal ethanol exposure. Thirty years later, new epidemiological and clinical studies as well as new biomarkers of fetal-alcohol damage have identified high risk populations and have provided data demonstrating that significant number of women in the EU drink during pregnancy. In September of 2009, a conference on 'ALCOHOL AND PREGNANCY' was organized sponsored by the Swedish Presidency of the European Union, to discuss political interventions in the EU concerning this question. I briefly summarize here the discussions, presentations and the prevention programs of some European countries. The main conclusion of the conference was that we need more information and prevention programs to improve prevention of the harmful consequences of alcohol consumption during gestation.

Read Full Article,
http://www.ncbi.nlm.nih.gov/pubmed/20549143

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PubMed, Nepal Med Coll J. 2009 Dec;11(4):268-71.

120) EFFECT OF MATERNAL ALCOHOL CONSUMPTION ON CEREBELLUM OF RAT PUPS: A HISTOLOGICAL STUDY

Ghimire SR, Saxena AK, Rai D, Dhungel S.
Department of Anatomy, Patan Academy of Health Sciences, Lalitpur, Nepal. rajjsat@hotmail.com

ABSTRACT
Consumption of alcohol during pregnancy results in fetal alcohol syndrome (FAS) in newborn affecting the central nervous system which is more sensitive to deleterious effect of alcohol. This study was

conducted to observe the histological alterations in cerebellum of rat pups born to alcohol consuming mother rats. Virgin female albino rats were given 20.0% (v/v) alcohol through oral route two weeks prior to mating and continued till the weaning of their offspring. On postnatal day 27 (PND27), rat pups were sacrificed. Their brains were collected and weighed. The cerebellums were isolated and processed for histological study. The diameter of Purkinje cell and width of molecular and granular layers of the cerebellar hemisphere were measured. Results showed significantly decreased brain weight in rat pups of experimental group when compared to control. The diameter of Purkinje cells, width of molecular and granular layers were also found to be decreased in the experimental group. These results suggest that the maternal consumption of alcohol affects the brain growth and induces significant alterations in the histological architecture of cerebellum of growing rats.

Link to the Article,
http://www.ncbi.nlm.nih.gov/pubmed/20635607

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NEWS AND PRESS

Motherisk

A. CURRENT STUDIES AT MOTHERISK: ALCOHOL USE DURING PREGNANCY

The Motherisk drug testing lab is developing a new screening test to determine prenatal alcohol exposure in newborns. The procedure involves lab analysis of meconium (the newborn's first stool after birth), that is collected from diapers.

This test is entirely non-invasive. The goal is to help physicians in the early identification and treatment of children who may be affected by heavy prenatal alcohol exposure. Health care and social service providers are strongly encouraged to refer pregnant women with a history of drinking to our lab. Women who abstained from alcohol during pregnancy can enroll as controls.

Participants will be asked to consent to the release of medical records pertaining to the pregnancy and the newborn, as well as the collection of a meconium sample directly from the infant's diaper. All data collected will be treated anonymously and with highest confidentiality for research purposes only.

Link to the Article,
http://www.motherisk.org/women/commonDetail.jsp?content_id=800

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Brookhaven National Laboratory News, 19th October 2010

B. FIRST DIRECT EVIDENCE THAT RESPONSE TO ALCOHOL DEPENDS ON GENES

UPTON, NY — Many studies have suggested that genetic differences make some individuals more susceptible to the addictive effects of alcohol and other drugs. Now scientists at the U.S. Department of Energy's (DOE) Brookhaven National Laboratory provide the first experimental evidence to directly support this idea in a study in mice reported in the October 19, 2010, issue of Alcoholism Clinical Experimental Research.

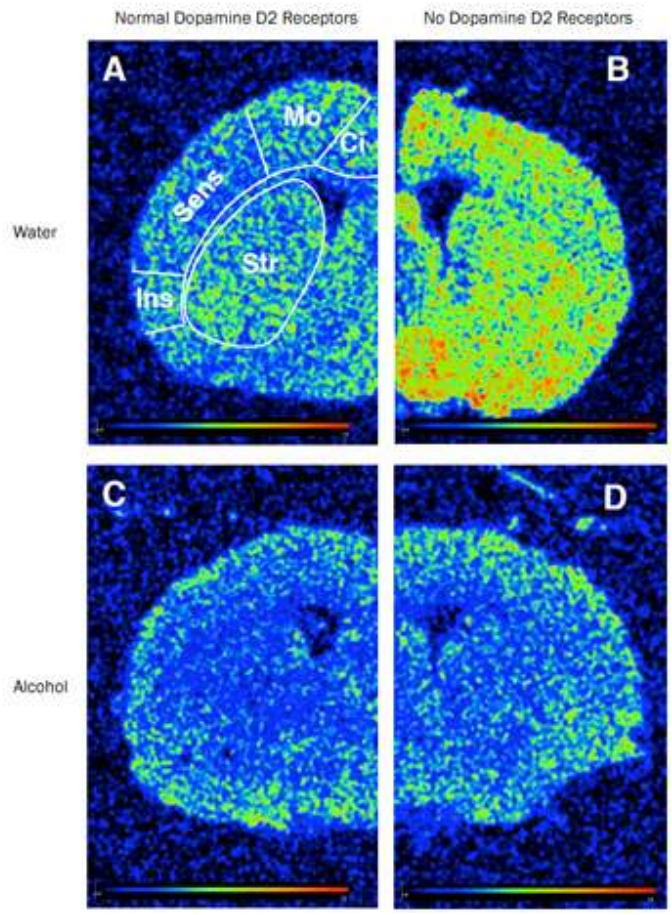
The study compared the brain's response to long-term alcohol drinking in two genetic variants of mice. One strain lacked the gene for a specific brain receptor known as dopamine D2, which responds to dopamine, the brain's "feel good" chemical, to produce feelings of pleasure and reward. The other strain was genetically normal. In the dopamine-receptor-deficient mice (but not the genetically normal strain), long-term alcohol drinking resulted in significant biochemical changes in areas of the brain well know to be involved in alcoholism and addiction.

"This study shows that the effects of chronic alcohol consumption on brain chemistry are critically influenced by an individual's pre-existing genetic makeup," said lead author Panayotis (Peter) Thanos, a neuroscientist with Brookhaven Lab and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) Laboratory of Neuroimaging. "Our findings may help explain how someone's genetic profile can interact with the environment — in this case, chronic alcohol drinking — to produce these changes only in some individuals, but not in others with a less vulnerable genetic profile. The work supports the idea that genetic screening could provide individuals with valuable information relevant to understanding risks when deciding whether or not to consume alcohol."

The scientists were particularly interested in the dopamine system because a wide range of studies at Brookhaven and elsewhere suggest that deficiency in dopamine D2 receptors may make people (and animals) less able to experience ordinary pleasures and more vulnerable to alcoholism, drug abuse, and even obesity. The ability to breed mice completely lacking the D2 gene — and carefully control and monitor their alcohol intake — made it possible to test the effect of this genetic influence on the brain's response to chronic alcohol drinking for the first time in this study.

The scientists studied mice lacking the dopamine D2 gene and genetically normal mice, all males. They divided these groups further, giving half of each group only water to drink, and the other half a solution of 20 percent ethanol to simulate heavy drinking.

After six months, the scientists compared the levels of a different kind of brain receptor known as cannabinoid type 1 (CB1) in various parts of the brain in all four groups. CB1 receptors are located near dopamine receptors and are also known to play a role in alcohol consumption and addiction. Many findings indicate that the two types of receptors may influence one another.



Levels of CB1 receptors in mice as measured by autoradiography, shown using a rainbow scale with blue representing the lowest levels and red the highest. Mice with no dopamine receptors drinking water (B) had higher levels of CB1 receptors than normal mice drinking water (A). Drinking alcohol seemed to negate this "up-regulation" in the

In the current study, the scientists found that water-drinking animals without D2 receptors had increased, or up-regulated, levels of CB1 receptors in brain regions associated with addiction, compared with water-drinking normal control animals. "That may mean that active D2 receptors in normal mice somehow inhibit the expression of the CB1 gene; and therefore, the absence of D2 leads to increased CB1 expression," Thanos said.

Chronic alcohol consumption, however seemed to negate this effect: D2-deficient mice that drank alcohol showed about half the CB1 levels compared to the D2-deficient water drinkers.

"We observed an up-regulation of CB1 in D2-deficient mice that was reversed by chronic ethanol intake," Thanos said. "This down-regulation of CB1 after alcohol intake in the D2-deficient animals could underlie the lower reinforcing effects of ethanol in these mice," he added.

Individuals experiencing lower-than-normal reinforcement, or reward, in response to a drug may be more likely than those experiencing a normal response to seek out further stimulation of the brain's reward centers by continued or increasing use of the drug.

To test this hypothesis, future research will explore the effects of CB1 down-regulation on animals' drinking behavior when given a choice between alcohol and water. The scientists will also conduct similar studies in female mice to investigate the role of gender on the observed findings.


Peter Thanos

"Further research on the relationship and interaction between genetic makeup and environment will help us better understand the chronic disease of addiction in terms of a series of risk factors that may elevate a person's vulnerability. This information will be imperative to the public and will help people make more informed decisions about their behaviors," Thanos said.

This research was funded by NIAAA. In addition to Thanos, who is jointly supported by Brookhaven Lab and NIAAA, co-authors include: Vanessa Gopez, Foteini Delis, and Gene-Jack Wang of Brookhaven Lab; Michael Michaelides of Brookhaven and Stony Brook University; David K. Grandy of Oregon Health and Science University; George Kunos and Nora Volkow, researchers from NIAAA.

All research involving laboratory animals at Brookhaven National Laboratory is conducted under the jurisdiction of the Lab's Institutional Animal Care and Use Committee in compliance with the Public Heath Service (PHS) Policy on Humane Care and Use of Laboratory Animals, the U.S. Department of Agriculture's Animal Welfare Act, and the National Academy of Sciences' Guide for the Care and Use of Laboratory Animals. This research has enhanced understanding of a wide array of human medical conditions including cancer, drug addiction, Alzheimer's and Parkinson's diseases, and normal aging and has led to the development of several promising treatment strategies.

Link to the Article,
http://www.bnl.gov/bnlweb/pubaf/pr/PR_display.asp?prID=1160

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The Daily Targum, 14th October 2010

C. RESEARCH EXPLORES EFFECTS OF ALCOHOL ON FETUSES

University animal science Professor Dipak Sarkar received a $3.5 million Method to Extend Research in Time award from the National Institutes of Health to expand support and funding for his studies on fetal alcohol syndrome for another decade.

The research focuses on two major disorders. Fetal alcohol syndrome is a pattern of physical and mental abnormalities that develop in unborn babies whose mothers excessively consume alcohol during pregnancy, said Sarkar, director of the Endocrine Research Program.

Fetal alcohol spectrum disorder, a broader term for a wide variety of health problems, includes fetal alcohol syndrome. It affects 2 percent of the population, he said.

"Those affected with fetal alcohol spectrum disorder face more stress problems than normal people," Sarkar said. "These people show signs of aggression, poor coping abilities, sleep disorder, infections and diseases, higher incidence of HIV and drug use."

The research suggests that drinking during pregnancy is more frequent among teenagers than older women, Sarkar said.

"Young people when pregnant often are not really taking care of their body, which is why they would drink. They are not exposed to the knowledge of drinking," he said.

For pregnant young women, the ignorance of even being with child often has tragic effects for their babies.

"Many teens don't even know that they are pregnant until they find out three or four months later, so by then, if they have been drinking, taking drugs or involved in other risky behaviors, their baby is at risk," said Francesca Maresca, a coordinator for Health Outreach, Promotion and Education.

Maresca said it is important to keep in mind that babies develop fetal alcohol syndrome through repeated long-term chronic exposure to alcohol while developing.

There are many new studies that show fetal alcohol toxicity causes a range of damages to the developing brain.

"Much of fetal alcohol toxicity to the [central nervous system] may occur in the second and third trimesters of pregnancy," said Nadka Boyadjieva, assistant research professor at the School of Environmental and Biological Sciences. "Those are very important periods when most other organs have already passed the stage of active organogenesis [organ development]."

Researchers found that exposure to ethanol may also lead to the early death of a fetus and affect the development of endocrine functions, such as those of the pituitary gland, thyroid gland, hypothalamus and pancreas.

"Offspring of mothers using ethanol during pregnancy are known to suffer from developmental delays and/or a variety of behavioral changes," Boyadjieva said. "Ethanol may affect the developing fetus in a dose-dependent manner and in different stages of development."

The researchers discovered many causes of fetal alcohol syndrome. One of the most important is that there are specific parts of the brain, mainly the hypothalamus, where abnormalities take place.

Beta-endorphin neurons in the brain are part of opioid, chemical transmitters found in the central nervous system, where they send signals throughout the body and control the immune system, Sarkar said.

"There are interactions between brain and immune system, and we have been studying the fetal alcohol effects on them," Boyadijieva said. "This area formed fetal alcohol disorders related to changes in both brain and immune system."

Endorphins are responsible for creating good moods and strengthening the immune system, but those with fetal alcohol syndrome have a deficiency in these biological painkillers, Sarkar said.

"For example, when you feel good after eating chocolate, your brain creates endorphins. These patients [affected by fetal alcohol syndrome] lack endorphins, leading to more hostile behaviors because they don't feel good," he said. "They have weaker immune functions, promoting a propensity to develop cancer, such as breast and prostate."

Research has shown that by artificially making new cells to produce endorphins, scientists can find a way to reduce symptoms and stress while improving health.

"Our idea of technology is taking stem cells to make them into endorphin neurons and insert them into the brain," Sarkar said. "We have tested this in animals and found out that it reduces stress, less drinking under stress and lower cases of cancer."

The research is 30 years in the making and researchers are at the preliminary stage, which entails giving alcohol to laboratory mice and rats, he said. They will need to conduct testing on larger animals and primates before they can test on humans.

Sarkar uses this research and stress biology in pursuit of a cure for fetal alcohol syndrome and fetal alcohol spectrum disorder. He is focusing on new manners of controlling bodily diseases and functions by manipulating the brain rather than the body itself.

"Information can be applied to those with depression and cancer who also have greater stress, less amount of endorphins and circadian rhythm sleep disorder even though they are not influenced by alcohol," Sarkar said.

Link to the Article,
http://www.dailytargum.com/science/research-explores-effects-of-alcohol-on-fetuses-1.2366600

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PR Newswire, 21st September 2010

D. DENTISTS HELP TO DETECT CHILDREN WITH FETAL ALCOHOL SPECTRUM DISORDERS

Certain Orofacial Characteristics Can Indicate the Condition

CHICAGO, Sept. 21 /PRNewswire-USNewswire/ -- Fetal alcohol spectrum disorders (FASD) is an umbrella term that describes the range of effects that can occur in a person whose mother drank alcohol while pregnant. Each year, FASD affect an estimated 40,000 infants in the United States—more than spina bifida, Down syndrome, and muscular dystrophy combined. Dentists have found themselves to be in a unique position to aid children with FASD because, oftentimes, they may see patients on a more frequent basis than a physician.

Defects caused by prenatal exposure to alcohol have been identified in virtually every part of the body. These areas include the brain, kidney, heart, ears, bones—and face. Dentists are now learning how to spot orofacial characteristics that often affect children with FASD, according to an article published in the September 2010 issue of AGD Impact, the monthly newsmagazine of the Academy of General Dentistry (AGD).

A thin upper lip, a smooth philtrum (the depression between the nose and upper lip), and a flat nasal bridge are all potential signs of FASD. In some cases, recognition of these specific orofacial characteristics can help lead to an accurate diagnosis, because other manifestations of FASD, particularly cognitive and behavioral ones, overlap with those of many other conditions, such as attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) and autism.

"Dentists are a critical part of each family's health care team and by learning the orofacial cues of FASD, not only can we provide the best care to children with the condition but also help the child's primary care physician to diagnose patients early on," says Peter G. Bastian, DDS, MAGD, spokesperson for the AGD. "An early diagnosis of FASD can improve the way in which the child's physician tailors the patient's treatments and visits to the office, as well as to improve the patient's

overall care. Because of their disabilities, patients with FASD often have special needs that require supportive services."

A proper diagnosis also aids the dentist in his or her patient treatment plan. "Oral challenges that dentists may face with children who have FASD include widespread cavities; mouth breathing caused by facial deformities, which leads to dry mouth; and jaw joint disorders," Dr. Bastian says.

The majority of children with FASD are diagnosed well after birth. While there is no cure for FASD, - people with FASD can still succeed with support programs and services, including special education, vocational programs, tutors, and structured environments, as needed.

FASD is 100 percent preventable when pregnant women abstain from alcohol. There is no known safe amount of alcohol to drink while pregnant. If you have questions about FASD, talk to your primary care physician and your dentist.

Link to the Article,
http://www.prnewswire.com/news-releases/dentists-help-to-detect-children-with-fetal-alcohol-spectrum-disorders-103442404.html

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LOW LEVEL STUDIES FROM AUSTRALIA AND THE UK AND CRITICAL REVIEWS

Since the publication of the 3rd issue of the FETAL ALCOHOL FORUM, the debate about the affect of low levels of alcohol has been back in the news. Two studies: one in the UK and one in Australia, according to the press, claim "mild drinking in pregnancy is OK, and may even be protective".

Because the debate about these studies has literally ricocheted around the world, we have devoted a section to both studies highlighting the press headlines and critical reviews from doctors and researchers.

UK STUDY

1) LIGHT DRINKING DURING PREGNANCY: STILL NO INCREASED RISK FOR SOCIOEMOTIONAL DIFFICULTIES OR COGNITIVE DEFICITS AT 5 YEARS OF AGE?
Kelly YJ, Sacker A, Gray R, Kelly J, Wolke D, Head J, Quigley MA.

- Press Headlines
- Full Study
- Crtiical Reviews and Responses

Press Headlines

"Light drinking no risk to baby, say researchers"
- BBC News (6th October 2010)

"Drinking wine while pregnant could help child's development"
- Express.co.uk (6th October 2010)

Light drinking during pregnancy 'does children no harm'
- The Guardian (6th October 2010)

Pregnant women told glass of wine a week won't harm baby: research
- The Daily Telegraph (6th October 2010)

Light Drinking said OK for Pregnant Women
- Discovery News (6th October 2010)

Light drinking during pregnancy does not harm child's behavioral or intellectual development
- Physorg.com (6th October 2010)

Mom's light drinking may not harm fetuses, study suggests
- The Globe and Mail (5th October 2010)

Full Study:-

Light drinking during pregnancy: still no increased risk for socioemotional difficulties or cognitive deficits at 5 years of age?

Yvonne J Kelly,[1] Amanda Sacker,[2] Ron Gray,[3] John Kelly,[1] Dieter Wolke,[4] Jenny Head,[1] Maria A Quigley[3]

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[2]Institute for Social and Economic Research (ISER), University of Essex, Colchester, UK
[3]National Perinatal Epidemiology Unit, University of Oxford, Headington, Oxford, UK
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Accepted 25 June 2010

ABSTRACT

Background This study examines the relationship between light drinking during pregnancy and the risk of socioemotional problems and cognitive deficits at age 5 years.

Methods Data from the nationally representative prospective UK Millennium Cohort Study (N=11 513) were used. Participants were grouped according to mothers' reported alcohol consumption during pregnancy: never drinker; not in pregnancy; light; moderate; heavy/binge. At age 5 years the strengths and difficulties questionnaire (SDQ) and British ability scales (BAS) tests were administered during home interviews. Defined clinically relevant cut-offs on the SDQ and standardised scores for the BAS subscales were used.

Results Boys and girls born to light drinkers were less likely to have high total difficulties (for boys 6.6% vs 9.6%, OR=0.67, for girls 4.3% vs 6.2%, OR=0.69) and hyperactivity (for boys 10.1% vs 13.4%, OR=0.73, for girls 5.5% vs 7.6%, OR=0.71) scores compared with those born to mothers in the not-in-pregnancy group. These differences were attenuated on adjustment for confounding and mediating factors. Boys and girls born to light drinkers had higher mean cognitive test scores compared with those born to mothers in the not-in-pregnancy group: for boys, naming vocabulary (58 vs 55), picture similarities (56 vs 55) and pattern construction (52 vs 50), for girls naming vocabulary (58 vs 56) and pattern construction (53 vs 52). Differences remained statistically significant for boys in naming vocabulary and picture similarities.

Conclusions At age 5 years cohort members born to mothers who drank up to 1–2 drinks per week or per occasion during pregnancy were not at increased risk of clinically relevant behavioural difficulties or cognitive deficits compared with children of mothers in the not-in-pregnancy group.

The link between heavy alcohol consumption during pregnancy and health and developmental problems in children is well established.[1] We recently reported that light alcohol consumption during pregnancy was not associated with an increased risk of behavioural difficulties or cognitive deficits at 3 years of age.[2] However, it is not clear whether these associations remain constant throughout childhood or change over time, and other work suggests possible 'sleeper' effects whereby developmental problems associated with maternal drinking during pregnancy may emerge later in childhood.[3 4]

In this paper we do two things to advance work in this area: first, we examine the relationship between light drinking during pregnancy and the risk of socioemotional problems and cognitive deficits at age 5 years; and second, we refine our analysis of maternal drinking during pregnancy by disaggregating the non-drinking category into two groups, those who never drink, that is 'teetotallers', and those who did not drink alcohol during pregnancy but otherwise drink. We used data from the Millennium Cohort Study (MCS).

METHODS

The Millennium Cohort Study

The MCS is a nationally representative longitudinal study of infants born in the UK. The sample was drawn from births in the UK between September 2000 and January 2002. The survey design, recruitment process and fieldwork have been described in detail elsewhere.[5] Briefly, 18 552 households agreed to participate in the first sweep of the survey, an interview response rate of 85%. Households were identified through the Department of Work and Pensions child benefit system and were selected on the basis of where the family was resident shortly after the time of birth. The sample has a probability design and is clustered at the electoral ward level such that disadvantaged residential areas are over-represented.

The first sweep of the survey involved home visits by interviewers when cohort members were aged 9 months. Questions were asked about mothers' drinking during pregnancy, other health-related behaviours, socioeconomic circumstances and household composition. Sweeps two and three of the survey took place when cohort members were aged approximately 3 and 5 years. At the age 5 years home visit cognitive assessments were carried out by trained interviewers and questions were asked about the cohort members' social and emotional behaviour, socioeconomic factors and the psychosocial environment of the family.

Ethical approval for the MCS was gained from the relevant ethics committees and parents gave informed consent before interviews took place, and separate written consent for cognitive assessments.

Mothers' drinking

During the first data sweep mothers were asked about whether they drank alcohol during pregnancy (every day, 5–6, 3–4, 1–2 days per week, 1–2 times per month, less than once per month, never). If the mother drank at least once or twice

per week she was asked: 'In an average week, how many units of alcohol did you drink?' If she drank once or twice per month or less than once per month she was asked: 'On the days when you did drink alcohol, on average how many units did you drink in a day?' Mothers were told: 'By a unit I mean, half a pint of beer, a glass of wine, or a single measure of spirit or liqueur.'

There are no widely agreed criteria on the levels of alcohol that constitute light or moderate drinking. We defined light and heavy/binge drinking on the criteria outlined by the National Alcohol Strategy.[6] Moderate drinking was defined as alcohol consumption at levels greater than light drinking, and less than heavy/binge drinking.

Another methodological concern comes from the observation that, in epidemiological studies drinking categories are heterogeneous in multiple ways. For example, in the current context non-drinkers are composed of mothers who never drink alcohol (so called 'teetotallers') and those that did not drink during their pregnancy but otherwise do drink alcohol. Moreover, in this particular context, if an experimental study design such as a randomised controlled trial were feasible, it would not necessarily make sense to include teetotallers in the study, and such a trial would only recruit participants who drank alcohol. In this scenario participants would be randomly assigned either to stop drinking or to be light drinkers. It follows that a more rigorous approach would be to refine the analysis of our observational data by disaggregating the non-drinkers into two groups: teetotallers and those who otherwise drink but not in pregnancy, and thus use the latter as the comparison group in multivariate analysis.

When cohort members were aged 9 months and 5 years mothers were asked about their current drinking patterns. We used these data to disaggregate the non-drinkers into two groups: never drinkers—reported not drinking in pregnancy, and when cohort members were aged 9 months and 5 years, and those who reported not drinking during pregnancy but did report drinking alcohol at the 9 month or 5 year interviews.

In this paper drinking categories are thus defined as follows:

- Never drinker (teetotallers)
- Not in pregnancy
- Light, not more than 1–2 units per week or per occasion
- Moderate, not more than 3–6 units per week or 3–5 units per occasion
- Heavy/binge, 7 or more units per week or 6 or more units per occasion.

Behavioural and emotional problems

When cohort members were approximately 5 years old, parents were asked to complete the strengths and difficulties questionnaire (SDQ) age 4–15 years version (http://www.sdqinfo.com). The SDQ asks questions about five domains of behaviour, namely: conduct problems; hyperactivity; emotional symptoms; peer problems and pro-social behaviour. The SDQ is a validated tool that has been shown to compare favourably with other measures for identifying hyperactivity and attention problems.[7 8] This paper focuses on aspects of behaviour, for example conduct problems and hyperactivity, previously linked to mothers' drinking during pregnancy.[3 9–14] Scores from the conduct problems, hyperactivity, emotional symptoms and peer problems subscales were summed to construct a total difficulties score. Clinically relevant cut points for problem behaviours were determined as the top 10% of all MCS children with SDQ data at age 5 years.[7] Cut points used were as follows: total difficulties ≥15; hyperactivity ≥7; conduct problems ≥4; emotional symptoms ≥4; peer problems ≥4.

Cognitive ability assessments

Cognitive ability at 5 years was assessed using widely validated, age-appropriate tests from the British ability scale (BAS): the naming vocabulary, picture similarities and pattern construction subscales.[15] The naming vocabulary subscale assesses expressive language and knowledge of names in English, the picture similarities subscale assesses pictorial reasoning and the pattern construction subscale assesses spatial skills. These subscales tap into the three most significant aspects of information processing: verbal reasoning, non-verbal reasoning and spatial abilities.[16] Mean age standardised T-score values for BAS subscales are reported. T-scores have a mean of 50 and SD of 10, and a range of 20 to 80. A cohort member with a T-score of 50 thus scored at the mean for the standardisation sample, while a cohort member with a T-score of 60 scored one SD above the mean and a cohort member with a T-score of 40 scored one SD below the mean for the standardisation sample. For the study sample gender-specific values were calculated for the mean and SD and these were used to generate Z-scores for each subscale. Z-scores were used in the analysis to aid model comparability.

Explanatory factors

Mother and infant, socioeconomic and family psychosocial factors that were hypothesised to confound or mediate the relationship between mothers' drinking and child behavioural and cognitive development were considered in explanatory models. Mother and infant confounding factors were: mother's age; number of children in the household at sweep 3; whether the pregnancy was planned; whether the mother smoked during pregnancy; the child's gender, birth weight and current age. Socioeconomic confounding factors were: highest parental occupation at sweep 1, highest parental educational qualification at sweep 1 and parental income at sweep 3. Family psychosocial markers hypothesised to mediate the relationship were from the sweep 3 interview: mother's current mental health (K6 questionnaire)[17]; parental discipline strategies (sum of frequency of ignoring, smacking, shouting, sending to the 'naughty chair', removing treats, telling off and bribing with response categories as never, rarely, sometimes ~1/month, often 1–6/week, daily); competence (whether the mother felt she was: not very good at being a parent; a person who has some trouble being a parent; an average parent; a better than average parent; a very good parent); closeness to the child (how close the mother felt to her child: not very, fairly, very, extremely) and whether the child was made to follow instructions (how often parent makes sure that child follows instructions or requests: never/almost never, less than half the time, more than half the time, all the time); and whether or not the mother currently drank alcohol.

Data analysis

Behavioural and cognitive outcomes and drinking in pregnancy are known to be moderated by ethnicity and multiple births.[18 19] Therefore we analysed data for all white singleton infants whose mothers participated in sweeps 1 and 3 of the MCS for whom data on drinking during pregnancy were available (n=12 294). Behavioural outcome data at age 5 years were available for total difficulties (n=12 079), conduct problems (n=12 161), hyperactivity (n=12 125), emotional symptoms (n=12 149) and peer problems (n=12 132). Cognitive test data were available for: naming vocabulary (n=12 110), picture similarities (n=12 099), pattern construction (n=12 059) cohort members. Missing data for explanatory factors of interest for behavioural outcomes reduced the sample to: total difficulties (n=11 450; 94.8%); conduct problems (n=11 511; 94.7%); hyperactivity (n=11 485;

Table 1 Mother, infant, socioeconomic and psychosocial markers by patterns of mothers' drinking during pregnancy

	Category of drinking				
	Never n=680	Not in pregnancy n=6935	Light n=2981	Moderate n=633	Heavy/binge n=284
Infant's gender, %					
Male	53.6	50.6	51.8	49.6	51.1
Birth weight (kg), (mean)***	3.368	3.395	3.449	3.413	3.325
Mother's age at time of birth (years), %***					
13–19	7.8	9.1	4.8	7.0	13.1
20–24	17.7	17.4	10.2	13.0	21.3
25–29	31.4	29.1	27.5	23.5	23.3
30–34	27.1	29.6	36.4	33.2	22.4
35–39	14.0	13.2	18.5	19.0	17.5
40 plus	2.0	1.6	2.6	4.4	2.4
No of children in the household, %***					
1	12.7	17.8	14.7	13.7	27.5
2	40.0	50.5	54.8	42.8	44.5
3+	47.3	31.7	30.6	43.4	28.0
Mother smoked during pregnancy, %***					
Yes	33.2	23.1	16.8	29.9	44.6
Pregnancy planned, %***					
Yes	50.9	57.7	65.4	52.4	48.1
Family income, %***					
£52 000 or more	4.1	8.6	16.6	13.7	8.1
£32 200–51 999	14.8	21.4	27.7	24.5	18.4
£20 800–32 199	20.0	23.9	21.0	19.1	18.5
£10 400–20 799	32.0	24.9	17.9	22.8	25.4
Less than £10 400	19.5	13.9	9.1	12.9	20.7
Don't know	8.5	5.6	5.9	4.9	8.3
Refused	1.2	1.7	1.8	2.2	0.5
Highest parental educational qualification, %***					
Higher degree	3.8	5.1	11.1	7.2	6.0
First degree/diploma	26.9	35.2	46.4	38.8	31.9
A/AS levels	15.5	18.0	15.2	14.2	18.6
GCSE grades A–C	31.2	28.1	20.1	25.5	27.0
GCSE grades D–G	5.7	6.2	3.4	4.2	6.7
Other/overseas	3.0	0.8	0.7	0.8	0.6
None	14.0	6.4	3.2	9.2	9.3
Highest parental occupation, %***					
Managerial and professional	11.9	19.0	32.9	25.3	19.8
Intermediate	10.7	12.8	14.0	14.0	11.5
Small employer and self-employed	6.3	8.1	10.6	8.8	8.1
Low supervisory & technical	10.2	11.0	9.0	6.0	10.2
Semi-routine and routine	55.1	46.0	31.6	42.0	43.6
Never worked, long-term unemployed and other unclassified	5.8	3.1	1.9	3.9	6.8
Mother currently drinks, %***					
Yes	0.0	92.4	96.3	94.1	94.2
Mother's K6 score, (mean) ***	3.4	3.0	2.9	3.2	3.2
Parental discipline, (mean)***	10.5	11.5	12.0	11.9	12.2
Mother's parenting competence, %**					
Very good	35.1	31.7	26.0	27.6	31.0
Better than average	21.9	27.9	32.7	31.1	25.8
Average	39.0	36.8	37.5	38.5	38.7
Some trouble	3.3	3.2	3.4	2.5	4.4
Not very good	0.7	0.4	0.3	0.2	0.2
Mother makes sure child obeys instructions, %					
All of the time	53.8	54.9	51.5	48.9	55.4
More than half of the time	24.0	29.4	35.0	32.7	29.7
About half of the time	12.8	9.1	9.2	11.7	7.9
Less than half of the time	7.1	4.9	3.2	5.5	5.6
Never/almost never	2.3	1.6	1.2	1.3	1.5
Mother's closeness to child, %*					
Extremely close	71.6	72.8	69.8	66.8	70.0
Very close	25.0	24.4	27.3	30.2	26.5
Fairly close	3.2	2.6	2.9	3.0	3.4
Not very close	0.2	0.2	0.1	0.0	0.1

*$p<0.05$; **$p<0.01$; ***$p<0.001$.

94.7%); emotional symptoms (n=11 503; 94.7%) and peer problems (n=11 481; 94.6%); and for naming vocabulary (n=11 370; 93.9%), for picture similarities (n=11 360; 93.9%) and pattern construction (n=11 330; 93.9%).

Cohort members whose families participated in MCS sweep 1 but not in sweep 3 were more likely to be from disadvantaged backgrounds. Their mothers were younger, more likely to be lone parents, and have lower incomes compared with mothers who took part in both sweeps (appendix 1).

Multivariate analyses are based on the cases with complete data on relevant variables using Stata version 11.0. The SVY command was used together with survey weights throughout to take account of the clustered sample design, the unequal probability of being sampled and survey non-response.

Logistic regression models were used to investigate the relative importance of mother and infant, socioeconomic and family psychosocial factors on the likelihood of behavioural difficulties in children according to mothers' drinking in pregnancy category. Linear regression models investigate relationships between mother and infant, socioeconomic and family psychosocial factors to cognitive ability scores. There were gender differences in behavioural problems and cognitive ability scores and so models are presented for boys and girls separately. We hypothesised that mother and infant and socioeconomic factors would confound the association between mother's drinking and child outcomes, whereas psychosocial factors would mediate this relationship, so adjustment was done separately for different types of factors. Behavioural outcome models adjust for age at sweep 3, cognitive outcome models do not as individual scores are age standardised. Model A shows the unadjusted associations, model B additionally adjusts for mother and infant factors, model C for socioeconomic markers, model D for family psychosocial environment and model E simultaneously adjusts for all factors.

RESULTS

A total of 5.9% of mothers never drank alcohol, 60.2% did not drink in pregnancy and 25.9%, 5.5% and 2.5% were categorised as light, moderate and heavy/binge drinkers, respectively. Light drinkers were more socioeconomically advantaged compared with mothers in all other categories. The socioeconomic profile of mothers in the 'not-in-pregnancy' group was more advantaged than the 'never-drinker' group but less advantaged than the 'light' drinking group (table 1).

Boys were more likely than girls to have high total difficulties (9.3% vs 6.0%), conduct problems (11.2% vs 7.9%), hyperactivity (12.8% vs 7.1%) and peer problems (7.3% vs 5.1%) scores. Girls were more likely to have high emotional symptom scores compared with boys (9.5% vs 8.7%). Girls had higher mean cognitive ability test scores compared with boys, naming vocabulary (56.3 vs 55.7), picture similarities (56.2 vs 55.1) and pattern construction (52.0 vs 50.4).

Boys and girls born to light drinkers were less likely to have high total difficulties (for boys 6.6% vs 9.6%, OR=0.67, 95% CI 0.53 to 0.86; for girls 4.3% vs 6.2%, OR=0.69, CI 0.50 to 0.96) and hyperactivity (for boys 10.1% vs 13.4%, OR=0.73, CI 0.58 to 0.91; for girls 5.5% vs 7.6%, OR=0.71, CI 0.53 to 0.94) scores compared with those born to mothers in the not-in-pregnancy group (table 2). These differences were attenuated on adjustment for mother and infant, and socioeconomic factors and in fully adjusted models.

Boys born to light drinkers had higher mean cognitive test scores compared with those born to mothers in the not-in-pregnancy group: naming vocabulary (57.5 vs 55.1), picture similarities (56.3 vs 54.6) and pattern construction (51.6 vs 50.0) and the differences for naming vocabulary and picture similarities remained statistically significant in fully adjusted models. Girls born to light drinkers compared with those born to mothers in the not-in-pregnancy group had higher mean scores on the naming vocabulary (57.6 vs 56.0) and pattern construction (53.0 vs 51.7) subscales, but differences were attenuated on adjustment for socioeconomic factors and in fully adjusted models (table 3).

DISCUSSION

Main findings

In this large nationally representative study of 5 year olds there appeared to be no increased risk of socioemotional difficulties or cognitive deficits in children born to light drinkers compared with children born to mothers in the not-in-pregnancy group. After adjustment for a range of confounding and mediating variables boys born to light drinkers had higher cognitive ability scores compared with those with mothers in the not-in-pregnancy group.

Strengths and limitations

We report findings from a large nationally representative sample of 5-year-old children, and these results are consistent with our previous work that suggested a U-shaped relationship between maternal drinking in pregnancy and developmental outcomes in 3-year-old children[2] and those from other studies.[11 20–22] The apparent U-shaped relationship between alcohol consumption and the risk of mortality and chronic disease in adults has been widely documented, and while the underlying relationship is not clear, it has been hypothesised that never drinkers are somehow different from others in their health and social profiles.[23] Data on drinking during pregnancy were collected when cohort members were aged 9 months, and although some studies report that retrospective recall of alcohol consumption is reliable,[24 25] it is possible that the measure used in this study was prone to recall bias. In addition, when not pregnant approximately 94% of our sample usually drank but only approximately 34% of mothers reported drinking during pregnancy, and it is not clear what proportion of women stopped drinking before conception or before pregnancy recognition. On the other hand, the current analysis also shows that children born to mothers in the heavy/binge drinking category were more likely to have hyperactivity, conduct and emotional problems compared with children born to mothers who did not drink during pregnancy, although cell sizes were small and statistical differences were attenuated on adjustment for confounding and mediating factors. This consistency with other studies[26 27] strengthens the validity of our findings.

The drinking categories used were heterogeneous in terms of the amounts of alcohol mothers reported consuming during pregnancy. We attempted to remove some of the inherent heterogeneity of the abstinent group by disaggregating into two groups: the teetotallers and those who did not drink during pregnancy but who otherwise did drink alcohol, and we used the latter as the baseline comparison group. Thereby, in terms of socioeconomic maternal and psychosocial profiles the baseline group were more comparable with the light drinking group than would be the case if the non-drinkers were combined. A clear strength of this study is that a wide range of hypothesised socioeconomic confounding and psychosocial mediating factors were accounted for in multivariate models. Children's social and emotional behaviours and cognitive abilities are heavily influenced by the social environment, and social gradients in markers of child development are evident.[28 29] The mechanisms through

Table 2 Prevalence (%) and OR (95% CI) for high behavioural difficulties scores

Boys	Prevalence	Model A		Model B		Model C		Model D		Model E	
Total difficulties, n=5864											
Never	14.6	1.61	(1.11 to 2.34)	1.51	(1.03 to 2.20)	1.31	(0.88 to 1.95)	1.27	(0.75 to 2.16)	1.29	(0.74 to 2.27)
Not in pregnancy	9.6	Ref		Ref		Ref		Ref		Ref	
Light	6.6	0.67	(0.53 to 0.86)	0.82	(0.64 to 1.04)	0.91	(0.71 to 1.17)	0.66	(0.50 to 0.85)	0.77	(0.59 to 1.01)
Moderate	10.7	1.15	(0.77 to 1.71)	1.19	(0.80 to 1.78)	1.32	(0.87 to 1.99)	1.07	(0.71 to 1.61)	1.10	(0.71 to 1.70)
Heavy/binge	15.7	1.76	(1.09 to 2.82)	1.40	(0.85 to 2.31)	1.63	(0.99 to 2.68)	1.86	(1.03 to 3.38)	1.63	(0.92 to 2.89)
Conduct problems, n=5896											
Never	14.8	1.42	(0.98 to 2.07)	1.27	(0.87 to 1.87)	1.18	(0.81 to 1.73)	1.45	(0.87 to 2.41)	1.50	(0.86 to 2.62)
Not in pregnancy	10.8	Ref		Ref		Ref		Ref		Ref	
Light	10.0	0.92	(0.74 to 1.15)	1.12	(0.89 to 1.40)	1.16	(0.93 to 1.45)	0.89	(0.70 to 1.14)	1.06	(0.83 to 1.35)
Moderate	14.7	1.43	(0.99 to 2.07)	1.45	(0.99 to 2.13)	1.59	(1.09 to 2.33)	1.32	(0.87 to 2.00)	1.34	(0.87 to 2.06)
Heavy/binge	18.1	1.82	(1.14 to 2.89)	1.51	(0.95 to 2.43)	1.69	(1.05 to 2.71)	1.82	(1.00 to 3.30)	1.55	(0.89 to 2.71)
Hyperactivity, n=5883											
Never	15.9	1.22	(0.84 to 1.77)	1.15	(0.79 to 1.67)	1.05	(0.71 to 1.57)	1.05	(0.67 to 1.65)	1.11	(0.69 to 1.78)
Not in pregnancy	13.4	Ref		Ref		Ref		Ref		Ref	
Light	10.1	0.73	(0.58 to 0.91)	0.86	(0.68 to 1.05)	0.90	(0.72 to 1.12)	0.69	(0.55 to 0.87)	0.81	(0.64 to 1.01)
Moderate	12.6	0.92	(0.61 to 1.39)	0.98	(0.64 to 1.48)	1.02	(0.68 to 1.54)	0.82	(0.54 to 1.23)	0.87	(0.57 to 1.34)
Heavy/binge	19.6	1.57	(1.05 to 2.34)	1.35	(0.90 to 2.02)	1.52	(0.99 to 2.31)	1.52	(0.95 to 2.43)	1.43	(0.91 to 2.26)
Emotional symptoms, n=5892											
Never	13.6	1.69	(1.16 to 2.46)	1.65	(1.12 to 2.43)	1.53	(1.03 to 2.27)	1.25	(0.73 to 2.12)	1.25	(0.72 to 2.17)
Not in pregnancy	8.5	Ref		Ref		Ref		Ref		Ref	
Light	7.4	0.87	(0.68 to 1.12)	0.97	(0.75 to 1.25)	1.01	(0.78 to 1.33)	0.90	(0.68 to 1.17)	0.95	(0.72 to 1.26)
Moderate	9.2	1.10	(0.67 to 1.80)	1.18	(0.73 to 1.91)	1.22	(0.74 to 2.01)	1.07	(0.65 to 1.75)	1.17	(0.71 to 1.93)
Heavy/binge	15.4	1.96	(1.18 to 3.23)	1.81	(1.08 to 3.02)	1.83	(1.10 to 3.06)	2.01	(1.14 to 3.56)	2.02	(1.16 to 3.52)
Peer problems, n=5882											
Never	10.9	1.46	(0.92 to 2.32)	1.37	(0.86 to 2.17)	1.22	(0.77 to 1.91)	1.29	(0.68 to 2.43)	1.20	(0.64 to 2.23)
Not in pregnancy	7.7	Ref		Ref		Ref		Ref		Ref	
Light	6.3	0.80	(0.62 to 1.03)	0.89	(0.69 to 1.14)	0.94	(0.73 to 1.21)	0.83	(0.64 to 1.08)	0.88	(0.68 to 1.15)
Moderate	5.2	0.66	(0.36 to 1.22)	0.65	(0.35 to 1.18)	0.71	(0.38 to 1.33)	0.62	(0.32 to 1.21)	0.62	(0.32 to 1.20)
Heavy/binge	5.6	0.71	(0.37 to 1.38)	0.59	(0.31 to 1.14)	0.62	(0.31 to 1.23)	0.70	(0.35 to 1.40)	0.59	(0.29 to 1.19)
Girls											
Total difficulties, n=5586											
Never	8.2	1.36	(0.82 to 2.25)	1.09	(0.64 to 1.87)	0.95	(0.57 to 1.59)	1.23	(0.60 to 2.52)	1.18	(0.54 to 2.58)
Not in pregnancy	6.2	Ref		Ref		Ref		Ref		Ref	
Light	4.3	0.69	(0.50 to 0.96)	0.88	(0.62 to 1.24)	1.01	(0.72 to 1.42)	0.67	(0.46 to 0.98)	0.89	(0.60 to 1.32)
Moderate	8.5	1.42	(0.92 to 2.20)	1.28	(0.82 to 1.99)	1.38	(0.88 to 2.16)	1.35	(0.85 to 2.14)	1.22	(0.74 to 1.99)
Heavy/binge	8.4	1.39	(0.68 to 2.85)	0.96	(0.45 to 2.04)	1.26	(0.58 to 2.74)	1.15	(0.56 to 2.37)	1.03	(0.47 to 2.27)
Conduct problems, n=5615											
Never	11.2	1.46	(0.97 to 2.21)	1.17	(0.77 to 1.79)	1.00	(0.64 to 1.59)	1.04	(0.55 to 1.96)	0.86	(0.45 to 1.67)
Not in pregnancy	7.9	Ref		Ref		Ref		Ref		Ref	
Light	6.6	0.81	(0.61 to 1.08)	0.99	(0.74 to 1.33)	1.13	(0.84 to 1.51)	0.81	(0.59 to 1.09)	1.00	(0.72 to 1.39)
Moderate	9.5	1.22	(0.80 to 1.86)	1.09	(0.71 to 1.66)	1.14	(0.75 to 1.73)	1.14	(0.67 to 1.91)	0.97	(0.57 to 1.65)
Heavy/binge	13.2	1.77	(1.01 to 3.11)	1.32	(0.70 to 2.48)	1.63	(0.86 to 3.07)	1.46	(0.79 to 2.72)	1.30	(0.64 to 2.62)
Hyperactivity, n=5602											
Never	8.7	1.16	(0.68 to 1.98)	1.01	(0.58 to 1.75)	0.82	(0.48 to 1.39)	0.72	(0.35 to 1.49)	0.67	(0.32 to 1.39)
Not in pregnancy	7.6	Ref		Ref		Ref		Ref		Ref	
Light	5.5	0.71	(0.53 to 0.94)	0.86	(0.65 to 1.15)	0.96	(0.72 to 1.28)	0.70	(0.52 to 0.95)	0.87	(0.64 to 1.18)
Moderate	7.0	0.92	(0.59 to 1.45)	0.88	(0.56 to 1.39)	0.91	(0.57 to 1.44)	0.84	(0.51 to 1.37)	0.83	(0.50 to 1.38)
Heavy/binge	10.2	1.38	(0.71 to 2.66)	1.04	(0.54 to 2.02)	1.28	(0.64 to 2.55)	1.19	(0.63 to 2.26)	1.05	(0.55 to 1.97)
Emotional symptoms, n=5611											
Never	12.1	1.29	(0.84 to 1.98)	1.17	(0.76 to 1.79)	1.07	(0.69 to 1.64)	1.28	(0.70 to 2.33)	1.26	(0.68 to 2.32)
Not in pregnancy	9.6	Ref		Ref		Ref		Ref		Ref	
Light	8.8	0.91	(0.72 to 1.16)	1.02	(0.80 to 1.29)	1.09	(0.86 to 1.40)	0.93	(0.72 to 1.19)	1.03	(0.79 to 1.34)
Moderate	9.6	1.00	(0.66 to 1.50)	0.95	(0.64 to 1.42)	0.98	(0.66 to 1.47)	0.96	(0.62 to 1.47)	0.93	(0.61 to 1.42)
Heavy/binge	9.9	1.01	(0.55 to 1.95)	0.91	(0.48 to 1.72)	0.96	(0.50 to 1.84)	0.92	(0.49 to 1.74)	0.89	(0.46 to 1.72)

Continued

Table 2 Continued

Boys	Prevalence	Model A		Model B		Model C		Model D		Model E	
Peer problems, n=5599											
Never	7.2	1.39	(0.80 to 2.43)	1.31	(0.75 to 2.31)	1.12	(0.63 to 1.98)	1.48	(0.72 to 3.03)	1.51	(0.72 to 3.19)
Not in pregnancy	5.3	Ref		Ref		Ref		Ref		Ref	
Light	4.2	0.78	(0.57 to 1.08)	0.88	(0.63 to 1.22)	0.97	(0.70 to 1.36)	0.79	(0.57 to 1.11)	0.91	(0.64 to 1.29)
Moderate	5.7	1.07	(0.56 to 2.05)	1.04	(0.54 to 2.01)	1.08	(0.56 to 2.07)	0.98	(0.51 to 1.89)	1.00	(0.52 to 1.91)
Heavy/binge	6.0	1.13	(0.49 to 2.64)	0.92	(0.39 to 2.14)	1.03	(0.43 to 2.48)	0.99	(0.43 to 2.29)	0.92	(0.40 to 2.12)

Model A adjusts for child's age.
Model B adjusts for child's age, birth weight, mother's age at time of birth, number of children in the household, mother smoked during pregnancy, pregnancy planned.
Model C adjusts for child's age, birth weight, parental income, highest parental educational qualification, highest parental occupation.
Model D adjusts for child's age, birth weight, mother's K6 score, parental discipline, child made to follow instructions, mother's parental competence, closeness of relationship between mother and child, mother's current drinking.
Model E adjusts for child's age, birth weight, mother's age at time of birth, number of children in the household, mother smoked during pregnancy, pregnancy planned, parental income, highest parental educational qualification, highest parental occupation, mother's K6 score, parental discipline, child made to follow instructions, mother's parental competence, closeness of relationship between mother and child, mother's current drinking.

Table 3 Mean and Z-scores (95% CI) for BAS cognitive ability tests

Boys	Mean test T-score	Model A		Model B		Model C		Model D		Model E	
Naming vocabulary, n=5815											
Never	51.3	−0.18	(−0.33 to 0.03)	−0.13	(−0.26 to 0.00)	−0.08	(−0.21 to 0.06)	0.00	(−0.18 to 0.18)	−0.02	(−0.18 to 0.14)
Not in pregnancy	55.1	Ref		Ref		Ref		Ref		Ref	
Light	57.5	0.23	(0.16 to 0.30)	0.15	(0.09 to 0.22)	0.09	(0.02 to 0.15)	0.20	(0.13 to 0.27)	0.08	(0.01 to 0.14)
Moderate	56.1	0.09	(−0.05 to 0.24)	0.08	(−0.07 to 0.23)	0.03	(−0.12 to 0.18)	0.08	(−0.06 to 0.22)	0.04	(−0.10 to 0.19)
Heavy/binge	55.9	0.07	(−0.13 to 0.27)	0.12	(−0.07 to 0.32)	0.10	(−0.09 to 0.29)	0.06	(−0.14 to 0.26)	0.08	(−0.11 to 0.26)
Picture similarities, n=5819											
Never	53.3	−0.14	(−0.27 to 0.00)	−0.12	(−0.24 to 0.01)	−0.09	(−0.22 to 0.05)	0.03	(−0.14 to 0.21)	0.00	(−0.17 to 0.18)
Not in pregnancy	54.6	Ref		Ref		Ref		Ref		Ref	
Light	56.3	0.16	(0.09 to 0.23)	0.12	(0.05 to 0.18)	0.07	(0.01 to 0.14)	0.15	(0.08 to 0.22)	0.08	(0.01 to 0.14)
Moderate	56.0	0.13	(−0.01 to 0.27)	0.11	(−0.03 to 0.25)	0.08	(−0.05 to 0.21)	0.13	(0.00 to 0.27)	0.09	(−0.04 to 0.23)
Heavy/binge	55.4	0.07	(−0.11 to 0.25)	0.10	(−0.09 to 0.28)	0.08	(−0.10 to 0.25)	0.08	(−0.10 to 0.26)	0.07	(−0.10 to 0.24)
Pattern construction, n=5796											
Never	49.1	−0.09	(−0.23 to 0.05)	−0.06	(−0.19 to 0.07)	−0.02	(−0.15 to 0.11)	0.06	(−0.13 to 0.24)	0.05	(−0.13 to 0.23)
Not in pregnancy	50.0	Ref		Ref		Ref		Ref		Ref	
Light	51.6	0.16	(0.09 to 0.23)	0.11	(0.04 to 0.17)	0.06	(−0.01 to 0.13)	0.14	(0.07 to 0.21)	0.06	(−0.01 to 0.13)
Moderate	50.7	0.08	(−0.06 to 0.21)	0.06	(−0.07 to 0.20)	0.02	(−0.12 to 0.16)	0.06	(−0.07 to 0.20)	0.04	(−0.10 to 0.18)
Heavy/binge	49.7	−0.02	(−0.23 to 0.18)	0.03	(−0.17 to 0.22)	0.01	(−0.19 to 0.21)	−0.01	(−0.22 to 0.19)	0.01	(−0.18 to 0.21)
Girls											
Naming vocabulary, n=5555											
Never	53.8	−0.23	(−0.38 to 0.08)	−0.14	(−0.28 to 0.01)	−0.10	(−0.23 to 0.04)	−0.10	(−0.29 to 0.08)	−0.06	(−0.24 to 0.11)
Not in pregnancy	56.0	Ref		Ref		Ref		Ref		Ref	
Light	57.6	0.16	(0.09 to 0.23)	0.09	(0.02 to 0.16)	0.02	(−0.05 to 0.09)	0.14	(0.07 to 0.21)	0.02	(−0.05 to 0.09)
Moderate	55.9	−0.01	(−0.15 to 0.13)	0.03	(−0.10 to 0.16)	−0.02	(−0.14 to 0.10)	0.01	(−0.12 to 0.14)	0.00	(−0.12 to 0.12)
Heavy/binge	54.3	−0.18	(−0.35 to 0.01)	−0.12	(−0.29 to 0.05)	−0.15	(−0.31 to 0.02)	−0.15	(−0.33 to 0.02)	−0.15	(−0.31 to 0.01)
Picture similarities, n=5541											
Never	56.0	0.00	(−0.15 to 0.15)	0.05	(−0.10 to 0.20)	0.08	(−0.06 to 0.22)	0.06	(−0.12 to 0.25)	0.09	(−0.09 to 0.28)
Not in pregnancy	56.0	Ref		Ref		Ref		Ref		Ref	
Light	56.7	0.07	(0.00 to 0.14)	0.04	(−0.03 to 0.11)	−0.01	(−0.08 to 0.06)	0.06	(−0.02 to 0.13)	−0.01	(−0.07 to 0.06)
Moderate	56.6	0.06	(−0.08 to 0.20)	0.09	(−0.05 to 0.23)	0.06	(−0.08 to 0.19)	0.07	(−0.07 to 0.21)	0.08	(−0.06 to 0.21)
Heavy/binge	54.4	−0.16	(−0.36 to 0.04)	−0.11	(−0.30 to 0.08)	−0.14	(−0.33 to 0.05)	−0.15	(−0.35 to 0.06)	−0.14	(−0.33 to 0.05)
Pattern construction, n=5534											
Never	50.0	−0.18	(−033 to 0.03)	−0.12	(−0.27 to 0.03)	−0.09	(−0.23 to 0.04)	−0.07	(−0.26 to 0.12)	−0.06	(−0.24 to 0.12)
Not in pregnancy	51.7	Ref		Ref		Ref		Ref		Ref	
Light	53.0	0.14	(0.07 to 0.20)	0.09	(0.03 to 0.15)	0.05	(−0.02 to 0.12)	0.12	(0.05 to 0.18)	0.05	(−0.01 to 0.12)
Moderate	52.3	0.06	(−0.07 to 0.19)	0.09	(−0.03 to 0.21)	0.06	(−0.05 to 0.17)	0.07	(−0.05 to 0.20)	0.08	(−0.04 to 0.19)
Heavy/binge	50.2	−0.16	(−0.35 to 0.03)	−0.09	(−0.28 to 0.10)	−0.12	(−0.31 to 0.06)	−0.14	(−0.33 to 0.06)	−0.11	(−0.29 to 0.08)

Model A is unadjusted.
Model B adjusts for birth weight, mother's age at the time of birth, number of children in the household, mother smoked during pregnancy, pregnancy planned.
Model C adjusts for birth weight, parental income, highest parental educational qualification, highest parental occupation.
Model D adjusts for birth weight, mother's K6 score, parental discipline, child made to follow instructions, mother's parental competence, closeness of relationship between mother and child, mother's current drinking.
Model E adjusts for birth weight, mother's age at the time of birth, number of children in the household, mother smoked during pregnancy, pregnancy planned, parental income, highest parental educational qualification, highest parental occupation, mother's K6 score, parental discipline, child made to follow instructions, mother's parental competence, closeness of relationship between mother and child, mother's current drinking.
BAS, British ability scales.

What is already known on this subject

The link between heavy alcohol consumption during pregnancy and health and developmental problems in children is well established. It has been reported that light alcohol consumption during pregnancy is not associated with an increased risk of behavioural difficulties or cognitive deficits in 3-year-old children. However, there may be 'sleeper' effects, whereby developmental problems associated with maternal drinking during pregnancy emerge later in childhood.

which the social milieu influence child development are complex but include the mental health of parents, interactions between care-giver and child and the learning environment (Kelly *et al*, unpublished findings).[30] In this study population light alcohol consumption during pregnancy is a marker of relative socioeconomic advantage. Given this, it is perhaps not surprising to find that in our paper and another recent report by Alati and colleagues[22] adjustment for socioeconomic markers did most to attenuate observed relationships between light drinking and developmental outcomes. Therefore, rather than the direct physicochemical nature of the intrauterine environment, it is likely that social circumstances[28–31] to a large part are responsible for the relatively low rates of subsequent behavioural difficulties and the cognitive advantage in children whose mothers were light drinkers.

Problem behaviours and cognitive deficits in early childhood have previously been shown to predict later behavioural and educational outcomes.[32 33] A strength of this study was that we examined data on objective measures, collected by trained observers, of cognitive ability for cohort members. On the other hand, data on child behaviour were only available from a parent report and it has been shown elsewhere that multi-informant measures are more reliable for the clinical identification of problem behaviours.[34] However, the SDQ is a validated tool, has been shown to discriminate cases diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, version IV,[35] and importantly we determined age-appropriate norms in the current study by using the large MCS cohort data rather than norms from a different age range. The cut points use the same greater than 90th percentile cut-off criterion for clinical relevance as used in the original norms.[7] However, future work may benefit from the use of more in-depth assessments of neuropsychological function.

CONCLUSION

The findings of this paper and our previous work[2] suggest that up to the age of 5 years there is no increased risk of poor socioemotional or cognitive developmental outcomes in children born to mothers who drank not more than 1 or 2 units of alcohol per week during pregnancy. However, causal inference based on observational data is limited, and further work to tease out aetiological relationships is needed.

What this study adds

At age 5 years children born to mothers who drank up to one to two drinks per week during pregnancy were not at increased risk of clinically relevant behavioural difficulties or cognitive deficits compared with children born to mothers who did not drink during pregnancy.

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Competing interests None declared.

Patient consent Obtained from parents.

Ethics approval Ethics approval for the MCS was gained from the relevant ethics committees.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Jones KL,** Smith DW, Ulleland CN, *et al*. Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet* 1973;**301**:1267–71.
2. **Kelly Y,** Sacker A, Gray R, *et al*. Light drinking in pregnancy, a risk for behavioural problems and cognitive deficits at 3 years of age? *Int J Epidemiol* 2009;**38**:129–40.
3. **Sayal K,** Heron J, Golding J, *et al*. Prenatal alcohol exposure and gender differences in childhood mental health problems: a longitudinal population-based study. *Pediatrics* 2007;**119**:e426–34.
4. **Streissguth AP,** Sampson PD, Barr HM. Neurobehavioral dose-response effects of prenatal alcohol exposure in humans from infancy to adulthood. *Ann NY Acad Sci* 1989;**562**:145–58.
5. **Dex S,** Joshi H. *Children of the 21st century: from birth to 9 months*. Bristol: The Policy Press, 2005.
6. **HM Government.** *Safe. Sensible. Sociable. The next steps in the National Alcohol Strategy*. London: Crown copyright, 2007.
7. **Goodman R.** The strengths and difficulties questionnaire: a research note. *J Child Psychol Psychiatry* 1997;**38**:581–6.
8. **Goodman R.** Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad Child Adolesc Psychiatry* 2001;**40**:1337–45.
9. **Sood B,** Delaney-Black V, Covington C, *et al*. Prenatal alcohol exposure and childhood behavior at age 6 to 7 years: I. Dose-response effect. *Pediatrics* 2001;**108**:1–9.
10. **Jacobson SW,** Jacobson JL, Sokol RJ, *et al*. Preliminary evidence of primary socioemotional deficits in 7-year-olds prenatally exposed to alcohol. *Alcohol Clin Exp Res* 1998;**22**:61A.
11. **Linnet KM,** Dalsgaard S, Obel C, *et al*. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. *Am J Psychiatry* 2003;**160**:1028–40.
12. **O'Connor TG,** Heron J, Golding J, *et al*. Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years. Report from the Avon Longitudinal Study of Parents and Children. *Br J Psychiatry* 2002;**180**:502–8.
13. **D'Onofrio BM,** Van Hulle CA, Waldman ID, *et al*. Causal inferences regarding prenatal alcohol exposure and childhood externalising problems. *Arch Gen Psychiatry* 2007;**64**:1296–304.
14. **Richardson GA,** Ryan C, Willford J, *et al*. Prenatal alcohol and marijuana exposure: effects on neuropsychological outcomes at 10 years. *Neurotoxicol Teratol* 2002;**24**:309–20.
15. **Elliott CD,** Smith P, McCulloch K. *British Ability Scales Second Edition (BAS II): administration and scoring manual*. London: NFER-Nelson, 1996.
16. **Hill V.** Through the past darkly: a review of the British Ability Scales Second Edition. *Child Adolesc Ment Health* 2005;**10**:87–98.
17. **Kessler RC,** Andrews G, Colpe LJ, *et al*. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychol Med* 2002;**32**:959–76.
18. **George A,** Hansen K, Schoon I. Child behaviour and cognitive development. In: Hansen K, Joshi H, eds. *Millennium cohort study second survey: a user's guide to initial findings*. London: Centre for Longitudinal Studies, University of London, 2007.
19. **Panico L,** Kelly Y, on behalf of the ETHINC team. Ethnic differences in childhood cognitive development: findings from the Millennium Cohort Study (abstract). *J Epidemiol Community Health* 2007;**61**:A36.
20. **Fried PA,** O'Connell CM, Watkinson MA. 60- and 72-month follow-up of children prenatally exposed to marijuana, cigarettes, and alcohol: cognitive and language assessment. *J Dev Behav Pediatr* 1992;**13**:383–91.
21. **Testa M,** Quigley BM, Eiden RD. The effects of prenatal alcohol exposure on infant mental development: a meta-analytical review. *Alcohol Alcohol* 2003;**38**:295–304.
22. **Alati R,** Macleod J, Hickman M, *et al*. Intrauterine exposure to alcohol and tobacco use and childhood IQ: findings from a parental-offspring comparison within the Avon Longitudinal Study of Parents and Children. *Pediatr Res* 2008;**64**:659–66.
23. **Corrao G,** Rubbiati L, Bagnardi V, *et al*. Alcohol and coronary heart disease: a meta-analysis. *Addiction* 2000;**95**:1505–23.

24. **Jacobson SW,** Chiodo LM, Sokol RJ, *et al*. Validity of maternal report of prenatal alcohol, cocaine, and smoking in relation to neurobehavioral outcome. *Pediatrics* 2002;**109**:815—25.
25. **Alvik A,** Haldorsen T, Groholt B, *et al*. Alcohol consumption before and during pregnancy comparing concurrent and retrospective reports. *Alcohol Clin Exp Res* 2006;**30**:510—15.
26. **O'Leary C,** Zubrick SR, Taylor CL, *et al*. Prenatal alcohol exposure and language delay in 2-year-old children: the importance of dose and timing on risk. *Pediatrics* 2009;**123**:547—54.
27. **Sayal K,** Heron J, Golding J, *et al*. Binge pattern of alcohol consumption during pregnancy and childhood mental health outcomes: longitudinal population-based study. *Pediatrics* 2009;**123**:e289—96.
28. **Kelly YJ,** Nazroo JY, McMunn A, *et al*. Birthweight and behavioural problems in children: a modifiable effect? *Int J Epidemiol* 2001;**30**:88—94.
29. **Sacker A,** Quigley M, Kelly YJ. Breastfeeding and developmental delay: findings from the Millennium Cohort Study. *Pediatrics* 2006:**118**;e682—9.
30. **Waldfogel J,** Washbrook E. Early years policy. *Paper prepared for Sutton Trust-Carnegie Summit: Social Mobility and Education Policy*, 2008. http://www.suttontrust.com/reports/summit_report.pdf (accessed 23 August 2010).
31. **Day NL,** Zuo Y, Richardson GA, *et al*. Prenatal alcohol use and offspring size at 10 years of age. *Alcohol Clin Exp Res* 1999;**23**:863—9.
32. **Spira EG,** Fischel JE. The impact of preschool inattention, hyperactivity, and impulsivity on social and academic development: a review. *J Child Psychol Psychiatry* 2005;**46**:755—73.
33. **Pihlakoski L,** Sourander A, Aromaa M, *et al*. The continuity of psychopathology from early childhood to preadolescence. A prospective cohort study of 3—12-year-old children. *Eur Child Adolesc Psychiatry* 2006;**15**:409—17.
34. **Goodman R,** Ford T, Simmons H, *et al*. Using the Strengths and Difficulties Questionnaire (SDQ) to screen for child psychiatric disorders in a community sample. *Br J Psychiatry* 2000;**177**:534—9.
35. **Klasen H,** Woerner W, Wolke D, *et al*. Comparing the German versions of the Strengths and Difficulties Questionnaire (SDQ-Deu) and the Child Behavior Checklist. *Eur Child Adolesc Psychiatry* 2000;**9**:271—6.

APPENDIX 1

Socioeconomic profiles of mothers lost to follow-up from sweep 1 of the MCS

	Complete data at sweeps 1 and 3	Lost to follow-up at sweep 3
Mother's drinking during pregnancy, %		
Never	63.3	68.3
Light	28.8	22.8
Moderate	5.5	5.8
Heavy/binge	2.4	3.1
Mother's age at the time of birth (years), %		
13—19	6.6	11.6
20—24	13.6	21.6
25—29	27.8	26.2
30—34	33.6	26.9
35—39	16.2	11.8
40 plus	2.2	2.0
Mother smoked during pregnancy, %		
Yes	20.6	28.7
Lone parenthood, %		
Yes	11.4	20.9
Family income, %		
£52 000 or more	7.6	5.5
£32 200—51 999	18.9	11.6
£20 800—32 199	23.3	16.4
£10 400—20 799	28.7	30.2
Less than £10 400	15.9	28.3
Don't know/refused	5.6	8.0
Highest parental educational qualification, %		
Higher degree	7.6	5.3
First degree/diploma	40.8	27.1
A/AS levels	16.8	16.7
GCSE grades A—C	24.5	29.4
GCSE grades D—G	4.6	8.0
Other/overseas	0.8	1.4
None	5.0	12.1
Highest parental occupation, %		
Managerial and professional	24.9	17.0
Intermediate	13.3	12.1
Small employer and self-employed	9.2	6.6
Low supervisory and technical	10.3	9.3
Semi-routine and routine	39.7	48.8
Never worked, long-term unemployed and other unclassified	2.5	6.2

Crtitical Reviews and Responses

NOFAS-UK Press Release:
14 October 2010

Much attention has recently been given to the study**:** ***Light drinking during pregnancy: still no increased risk for socio-emotional difficulties or cognitive deficits at 5 years of age?*** by Yvonne J Kelly, Amanda Sacker, Ron Gray, John Kelly, Dieter Wolke, Jenny Head, Maria A Quigley (attached).

Thank you for your interest in the important issues raised by this study.

For your information, I have also attached a link to Dr Kelly's interview on BBC Radio. (http://www.bbc.co.uk/news/health-11476456) On the site, you will find the podcast in the audio box on the right toward the bottom of the article.

As the founder of NOFAS-UK and our Medical Advisory Panel, and the adoptive mother of a child with Fetal Alcohol Syndrome, I met recently with Dr Kelly to discuss her conclusions. Dr Kelly made it quite clear to me that ***the study does not imply that drinking is without risk***.

It is important to point out that this study is provisional, in that it followed children only to five years of age. Dr Kelly is in the process of completing a new study of the children at the age of seven, and that will provide further evidence, either confirming or modifying Dr. Kelly's conclusions. Until full longitudinal studies of the cohort are complete into adulthood, all conclusions must remain provisional.

In the meantime, NOFAS-UK supports and reiterates the Department of Health guidance for best practice: "Avoid alcohol when pregnant or if trying to conceive."

NOFAS-UK further supports all research that can improve evidence and increase information about alcohol and pregnancy.

Susan Fleisher
Executive Director
NOFAS-UK
The National Organisation for Fetal Alcohol Syndrome-UK

Pregnancy-and-drinking study draws fire
Anne McIlroy
Globe and Mail Update
Posted on Friday, October 8, 2010 4:37PM EDT

A controversial study published this week that suggested light drinking may not harm fetuses has drawn criticism from other researchers, including **Sterling Clarren** at the University of British Columbia.

There were a number of serious issues with the research, says Dr. Clarren, including that the children were assessed at the age of five, too early to see some of the problems that can be caused by exposure to alcohol.

But while pointing out the deficiencies of the work, Dr. Clarren adds that it is time for scientists to come up with better advice for pregnant women than the current public health warning of „no exposure equals no risk.‰

„We also know in our hearts of hearts, that certainly small amounts of alcohol delivered occasionally is safe. We all know that it bothers women that they are doing something that on some level they know is safe and yet the public healthy warning is different than that,‰ says Dr. Clarren, an expert in fetal alcohol spectrum disorders and CEO of the Canada Northwest FASD Research network,

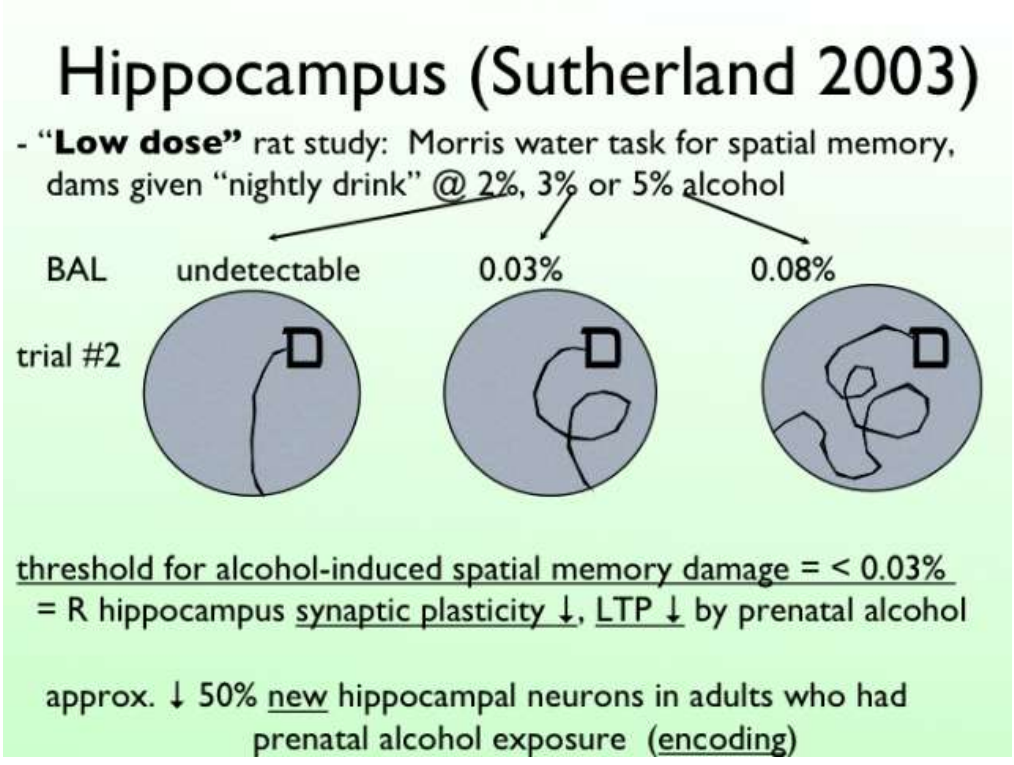
„The problem is the complexity of the issue. What is a drink? People don,t drink standard drinks. People don,t realize what they are drinking in absolute terms. How big is the person, 5 feet tall 100 pounds or 6 feet tall, 200 pounds? Do they have a lean body mass or a lot of body fat? Those all vary the distribution of alcohol.‰

There are so many, factors, he says, it becomes difficult to make a simple warning statement. One option is to set the bar very low, to say that a single drink once a month, is probably okay most of the time.

But first, he says, there needs to be social marketing research done to see how pregnant women would respond to a more nuanced message. Would they feel it was okay to indulge more regularly?

Rod Densmore, M.D.

Alcohol is a known teratogen. So is radiation such as Xrays. We'd never try to prove that a certain dosage of xrays was safe and a higher dose was unsafe. To do such a study would be unethical.



BAL is blood alcohol level
LTP is long term potentiation--that means laying down a new memory
trial #2 is the rodent has already found the platform (the little box in the slide---that was trial #1 so now he/she knows where the platform is and where the reward is--so under "undetectable " you can see our little rodent buddy swam straight to the submerged platform and got his reward. --the little guy whose mum had blood alcohol levels of .03% followed a circuitous route but eventually found the

platform--diagnosis : lousy short-term spatial memory--the little guy whose mum had .08% blood alcohol level was much worse.

So let's look at Dr. Sutherland's rodent study, above. He fed very modest doses of alcohol to rodent mums and assessed their offspring for spacial memory using the morris water test which is a standard spatial memory test--the human equivalent of getting lost on the way to the corner store. He fed his rodent mums the equivalent of the legal limit--.o8%, about a half of that, and about a third of that amount of alcohol. We know that even at blood alcohol levels of .03% which is less than half the legal limit the offspring's spatial memory was still impaired--that's the same as a bit less than one drink (i.e. 12 ounces of 5% beer) for a human.

Conclusion less than .03% i.e less than the human equivalent of a 12 ounce beer per night appears to be the threshold for spatial memory damage in this rodent model.

It is just beyond my comprehension why there is still discussion about trying to determine a safe threshold for liquor in pregnancy--the only logical reason i can think of is perhaps someone in the drinks industry is trying to cast doubts on the science. People planning pregnancy or pregnant should not drink. Those who disagree should review Dr Sutherland's carefully conducted study at:
Sutherland, RJ. (2003) Prenatal alcohol exposure neuropathology and cognition: integrating behavioral and neural approaches in rats and humans. Presented at Fetal Alcohol Canadian Expertise 2003 Meeting. downloaded from
http://www.knowledgenetwork.ca/fasii/index.html

From Science Media Centre, New Zealand

Dr Pat Tuohy, Chief Advisor – Child & Youth Health, Population Health Directorate, Ministry of Health, NZ comments:
“I have major criticisms of the conclusions in the attached press release drawn from this paper. The Authors themself were a lot more circumspect in their conclusions. Basically it confirms that if there are any adverse effects from drinking small amounts of alcohol during pregnancy they are subtle and not easy to find in a study like this. The paper only applies to women of European ethnicity, as other ethnic groups were excluded from analysis. It is subject to a range of biases and confounding factors. It does not show that drinking during pregnancy is better for your baby.

Specifically:
“1 There is clearly a confounding effect of socioeconomic status and maternal capability, self efficacy etc (however measured) on these results. i.e. brighter, better off, more capable mothers have similarly capable children. This is shown by the trend towards statistical non-significance as these confounding factors are entered into the statistical model. (Models A-E generally show a decreasing OR as you enter more confounders, indicating that the confounders are likely to be the major explanation for the findings). The study provides no explanation of why the ORs for teetotalers are so much higher on many scores. Surely this points to an unrecognised confounder.

“2 The actual Odds Ratios for the SDQ scores fail to reach significance in model E (The best corrected for confounders) except for the increase in emotional symptoms in the children of heavy/binge drinkers, which is not a surprising finding. All the other ORs include 1, which means that they are non-significant findings.

“3 Similarly the Z score confidence intervals in Table 3 all include zero (indicating a non significant effect) except for the light drinkers group for naming vocab, and picture similarities. However the CIs for these two criteria are both 0.01 to 0.14, so while statistically significant are only of marginal significance. However it is clear that the outcomes are not worse for these outcomes.

"My response on reading the paper is that the widely different numbers in the different exposure groups are going to give different weightings to the confidence intervals. This means that with only 284 mothers in the heavy/binge drinkers group the power of the study to show a real effect of alcohol using these tests is small, but with almost 3000 in the light drinking group it will be easier to show a real effect. The fact that a behavioural effect was shown in the children of heavy/binge drinkers on the SDQ is therefore quite significant, and probably meaningful. An indicator of the lack of power of this study to detect significant clinical differences is the lack of adverse outcomes in the IQ scores of children of heavy/binge drinkers – we would have expected to see that finding.

"The choice of the SDQ as the mental and emotional health test is a problem, because although it has a high-ish concordance with DSM IV assessments (about 0.75) it is a screening tool, not diagnostic. It is also not as sensitive or specific if a single informant (parent only) is used, as was the case here. The mental health and behavioural consequences of mild FASD are subtle and may not be identified well by the SDQ. The researchers recognised that parental ethnicity is an potential confounding factors but chose to exclude motehrs of 'non-european' ethnicity instead of attempting to correct for this confounder. – not clear why. Also 'higher risk' mothers are excluded from the analysis, as they were less likely to participate in the 5 year old sweep.

Our advice:
"We continue to advise that no alcohol in pregnancy is the best option. This study will however provide some reassurance to mothers who drank lightly in early pregnancy, and will reinforce that it is never too late to stop."

Dr Helen Moriarty, senior lecturer and addiction medicine practitioner, primary health care and general practice, University of Otago, Wellington, NZ comments:
"On the face of it this interesting paper would seem to challenge existing advice. However, there are flaws which cast doubt on the findings. Firstly it was a retrospective survey. Women were first asked about their drinking during pregnancy 9 months after the pregnancy had ended.

"Secondly there are numerical issues that the authors failed to address: the initial (9 month) survey was of 18,552 women which was an 85% response rate therefore the real bottom line is 21,825 (true denominator). That 15% would have refused to participate at all immediately raises a query since the drinking habits of these refusers is not known and the outcome on their children was not measured.

"Further problems with numbers appear in table 1 where data is reported for only 11,513 women (less than 53% of the 21,825). Subsequent results on behaviour outcomes etc only account for 11,374 (52% of 21,825). There were issues with missing data on the key outcome measures, ie incomplete data sets for all boys and girls. I think enough said from me. It will be a good paper to use to teach students about critical appraisal!"

Dr Sheryl Parackal, research fellow, School of Population Health, University of Auckland, NZ comments:
"1. The results observed in this study is limited to the outcomes measured in the study and hence in no way can imply that there are "NO effects" for light or any drinking in pregnancy.

"2. The result that children born to light drinkers are better off than children born to women "who stopped drinking in pregnancy" is not surprising because the majority of those who stopped in pregnancy are likely to have done so after "recognizing pregnancy", which could be any time from 4 weeks to 8 weeks or even later.

"The findings of our NZ study (Alcohol in pregnancy study 2005) indicates ~ half of women who were pregnant at the time of the study had drunk alcohol before realising they were pregnant and a high

proportion of these women had binged in this period. For most women, pregnancy starts when they realise they are pregnant and hence don't report drinking prior to this unless probed/asked. So the reference group used for the comparisons may not be appropriate."

Dr Rosemary Marks, developmental paediatrician at Auckland's Starship Hospital and President of the Paediatric Society of New Zealand comments:
"The cohort members' infants in this study were aged 9 months when the questions were asked about mothers drinking during pregnancy. One of the crucial times in relation to alcohol and pregnancy is the first few weeks after conception. You are asking people to recall what they were drinking 18 months ago when they may not have been aware they were pregnant. It is a difficulty which plagues all studies on this.

"Most women are well aware these days that there is concern about drinking in pregnancy, so there is an incentive to show yourself in a good light, a tendency to minimise the amount of drinking reported. That is a potential confounder, getting truthful information about how much people actually did drink.

"There was a very clear relationship between smoking and the drinking categories. Women who never drank actually had quite a high rate of smoking. Women who were light drinkers had the lowest rate of smoking. In the analysis, smoking was grouped with a number of other variables. Could the small differences between the groups have been explained by smoking rather than drinking?

"When you use 'not in pregnancy' as a reference point, you may have a problem there. Does 'not in pregnancy' mean anytime from conception onwards or does it mean 'not once you knew you were pregnant'?

"The advice that has always been given is that we do not know whether any drinking in pregnancy is safe or not and therefore until we have that information the advice is not to drink. The study doesn't contradict the advice given, it says it is probably not harmful so pregnant mothers who have the odd glass of wine can be slightly reassured that they are not doing their children harm."

Dr Trecia Wouldes, senior lecturer, psychological medicine at School of Medicine, University of Auckland, NZ comments:
"Kelly and colleagues have published further findings from the large Millenium Cohort Study that suggest children born to mothers defined as "light" drinkers were not at increased risk for clinically relevant behavioural or early learning difficulties.

"However, as with their earlier study of 3-year-old children, the findings from this follow-up study of 5-year-olds should be interpreted with caution as findings in both studies also show that "light" drinkers were more socially and economically advantaged than non-drinkers. This means children of "light drinkers" may have had better antenatal and postnatal care and live in environments where parents are better educated and there are more resources to support optimal cognitive and behavioural development."

"In addition, as the authors have pointed out there are a number of methodological limitations to their study that make it difficult to interpret these results. First, because of the way they have defined "light" drinking this category may have included a heterogeneous group of mothers who may have had 1 or 2 drinks during their entire pregnancy and mothers who consumed 1 or 2 drinks per week throughout their pregnancy.

"In order to have any confidence in the level of alcohol exposure to children in the "light" group, measures of absolute alcohol and the timing across trimesters of maternal consumption is needed. In addition, maternal reports of alcohol consumption were obtained at 9 months after birth requiring the mother to reconstruct from memory her drinking behaviour.

"Second, the developmental outcomes these researchers have reported were all based on questionnaires or reports provided by the mother. Independent evaluations of these children by preschool teachers or observations from developmental specialists using more in depth and comprehensive measures of behaviour and learning may have strengthened or negated their findings. Finally, although epidemiological studies can provide important information about maternal drinking patterns in women that is representative of the larger population, they usually do not have the resources to investigate in detail the environmental context of that drinking or the timing and frequency of alcohol, tobacco and other drug use during the pregnancy. Indeed the authors have noted in their discussion of the findings (p. 7), that given the impact of social advantage found in this and other studies of mothers who also reported light drinking, it is likely that "…rather than the direct physiochemical nature of the intrauterine environment it is likely that social circumstances to a large part are responsible for the relatively low rates of subsequent behavioural difficulties and the cognitive advantage in children whose mothers were "light" drinkers."

Professor Jennie Connor, Head of Department, Preventative and Social Medicine, Dunedin School of Medicine, University of Otago, NZ comments:
"The evidence of "safety" as well as the evidence of "harm" that comes from this study may be affected by a number of shortcomings of the cohort study design in answering questions about cause and effect. There is no way to completely eliminate the effects of other lifestyle factors, which are associated with different drinking patterns, on the outcomes for the children.

"Women who drink at a low level during pregnancy have other characteristics that make their children at less risk of the "problems" being studied, and women who drink heavily during pregnancy are very likely to have other characteristics that put their children at risk of these problems. The investigators have adjusted the results for some of these factors but cannot adjust for them all.

"When the results that are adjusted for all of the factors that they have data on (Model E in Table 2), the findings are not statistically significant. This means that it is plausible that there is no difference between the children of light drinkers and non-drinkers in terms of behavioural problems. The authors acknowledge all of these issues.

"I consider that the claim made in the press release that "Children born to light drinkers were 30% less likely to have behavioural problems than children whose mothers did not drink during pregnancy" is not supported by the data presented in the paper. Once the comparisons are adjusted for some of the other differences between the mothers, the difference is not 30% and not statistically significant. The authors do not appear to make this claim in the paper.

"As well as this source of bias in the results (confounding), alcohol studies require drinking data to be self reported, and in this study data were collected 9 months after the child's birth. Alcohol consumption is almost always under reported, and this measurement error is exacerbated when recall over long periods is required. So if the findings were true, there is no way of knowing what the true "safe" dose is.

"These problems do not mean the study was poorly carried out; they are inherent in the design. There are well known examples of results from cohort studies being found to be wrong when a randomised trial has been subsequently conducted on the same question. In this case the definitive study would require randomly allocating pregnant women to different levels of drinking during pregnancy and measuring the effects on the children, which would be clearly unethical.

"It is biologically unlikely that a moderate dose of alcohol would improve brain function in a fetus and a heavier dose would impair it, since alcohol is well known to be a neurotoxin.

“The authors say in the last paragraph “However, causal inference based on observational data is limited, and further work to tease out aetiological relationships is needed. This means that we cannot draw the conclusion that drinking in pregnancy is safe from this study.

“The most important message of the study is: Children of mothers who drank 7 or more units per week (one bottle of wine over the week) or 6 units at one sitting were more likely to be hyperactive, and have behavioural and emotional problems than children whose mothers chose not to drink during pregnancy.

“This is the most important message because we must take a precautionary approach to this issue. There will be individual variation in the effects of alcohol on the fetus and/or lack of clarity about the dose and or timing of alcohol exposure that can cause harm. There is no risk associated with abstinence.”

Dr Susan Morton, principal investigator, Growing Up in New Zealand longitudinal Study, University of Auckland, NZ comments:
“The Millenium Cohort Study is an important observational population longitudinal study that is looking at how children develop in the UK in the 21st century. However it did collect its first set of data from mothers when their children were at least 9 months of age. Hence the information collected about maternal drinking in pregnancy is subject to recall bias (because it is collected after the time when the drinking occurred and after the child had been born).

“It seems that there was also only one question asked of mothers about their frequency of drinking in pregnancy and mothers were not asked about when and how much they may have drunk at different stages of their pregnancy, particularly in the first trimester as compared to later in the pregnancy.
“This is especially important for planned and unplanned pregnancy (approximately 50% pregnancies reported to be unplanned) where heavy drinking at pre-pregnancy levels may continue into the first critical weeks of fetal development before a pregnancy is recognized. Further the assignment of ” never drinkers” in the MCS seems to rely on reported information from mothers only after their children were born rather than reflecting the situation before they were pregnant, which may have introduced further bais if mothers habits had changed after the birth of their children.

“In New Zealand currently mothers are advised to abstain from alcohol during pregnancy because (as Dr Connor points out) of the potentially harmful effects of heavy alcohol consumption. What is not well understood is what effects if any (on child development) lighter or more moderate drinking might have on children’s outcomes at birth and beyond. Because of this lack of scientific evidence about cause and effect we err on the side of caution and recommend that women abstain completely – as we know this is “safe”.

“Clearly conducting a scientific experiment to ascertain whether any level of drinking in pregnancy is safe or not would be unethical, therefore we do rely on observational, self-reported data to help us understand this issue further.

“To help to address this issue for our current New Zealand population the Growing Up in New Zealand longitudinal study has asked mothers and their partners about their drinking before and during their pregnancy at the first interview with over 7000 parents of the children in the new cohort. In contrast to the MCS we have asked the mothers and partners about their drinking when they were still pregnant, and have asked them to describe their drinking at each stage of their pregnancy (first trimester and beyond) as well as to compare this to their usual pre-pregnancy alcohol intake. The first results from these interviews are currently being prepared for release and will be available at the end of November (being released at parliament on November 25th).

“This is the first longitudinal study in New Zealand that has recruited both mothers and partners during pregnancy (to follow over 7000 children from before birth until they are young adults) and that has recruited a cohort that are representative of all our current births (so include Maori, Pacific and Asian parents and children in sufficient numbers in addition to our European parents and children). The information we have collected in this new study will allow us to see what effect different frequency and timing of alcohol intake has on our children as they grow up in New Zealand today.”

“As well as collecting information about alcohol intake the Growing Up in New Zealand study has also collected a wealth of information about the parents, their families and the environments into which the children have been born. This will allow us to consider the relationship between drinking in pregnancy and child development in the context of all the other behaviours and influences that may confound (also contribute to) any association that is seen.

“This is extremely important as mothers who have different patterns of alcohol consumption are also likely to differ in other significant ways that may affect their child’s growth and development (for example we will also be able to concurrently consider mothers and partners smoking during pregnancy, mothers nutrition, parents education and other markers of family circumstances and deprivation during pregnancy and after the children are born).”

Barry Stanley, MB Ch.B, F.R.C.S.[C]

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6th. October, 2010.

Light drinking during pregnancy: still no increased risk for socioemotional difficulties or cognitive deficiencies at 5 years of age? Y. J. Kelly et.al. Journal of Epidemiology and Public Health. October, 2010.

The SDQ is only a brief screening tool. It is questionable that its reliability extends to the highly charged questions of alcohol consumption during pregnancy and the effects on the child. The BAS is not comprehensive “were more specific abilities need investigating other diagnostic scales can be used to provide more detail"

FASD [fas and arnd] is truly a spectrum from the death of the fetus to the articulate, intelligent individual who never the less has the secondary disabilities of FASD to varying degrees. The secondary disabilities are drug and alcohol problems, incomplete schooling, confinement, difficulty maintaining employment and living independently. In addition 94% will eventually be given mental health diagnoses.

In order to identify the less effected all domains of brain function need to be evaluated, with subtests.

I have seen many times adolescents and adults who are articulate and intelligent yet have chaotic lives impacting others and society in general. They were never fully evaluated but when they are, as above, then significant deficiencies of brain function are found that account for their difficulties.

The evidence is that the sooner the effects of alcohol on the developing fetus is established the less

the secondary disabilities.

There is research that shows low levels of alcohol exposure cause deficiencies in brain function. It is true the research is limited; a reflection of denial by the majority of politicians and professionals.

Although the MCS is an ongoing longitudinal study I am left with the distinct and alarming impression that the two papers to date, and the response of the media, promote the consumption of alcohol during pregnancy rather than the urgent need for more research into the effect on the developing fetus of low levels of alcohol.

Finally I will leave your readers with a question. If it is all right to expose the fetus to alcohol during pregnancy is it all right to give the same amount of alcohol to the infant?

References provided on request.

Barry Stanley, MB Ch.B, F.R.C.S.[C]

Further to my letter of 6th October, 2010.
Re. Light drinking during pregnancy: still no increased risk for socioemotional difficulties or cognitive deficiencies at 5 years of age? Y.J. Kelly et.al. Journal of Epidemiology and Public Health. October, 2010.

The paradox of low alcohol consumption associated with higher brain function than average.

The most likely explanation for this conclusion is the plasticity of the brain. Animal models and limited research on infants and young children show that sensory motor stimulation and integration can improve cognition etc. in those diagnosed with FASD.

In my experience as the child grows it rapidly loses this ability and FASD is then essentially a permanent neurological condition.

In the "intelligent" older person with fasd a full neuropsychological assessment will often show percentiles in the mid to high nineties, with other domains of brain function at percentiles 2 to 20. It would seem that in these individuals there has been a increased process in some areas to compensate for the deficiencies in other areas as the brain was developing.
[This plastic process is an accepted neurological fact]

In such cases the individual child, from 3years to 6years, may present as above the average "intelligence", especially when the assessment of brain function was limited. Later, often to late to improve the person's life, the impact of the alcohol exposure becomes apparent and can be confirmed by a full neuropsychological assessment.

An extreme example would be the savant- brilliant in one area of brain function but extremely disabled in the rest of brain function.

The implications are that the earlier the diagnosis is made and the correct environment provided the more the secondary disabilities will be mitigated - an observation first made fourteen years ago.
Barry Stanley,

References provided on request

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AUSTRALIAN STUDY

2) LOW-MODERATE PRENATAL ALCOHOL EXPOSURE AND RISK TO CHILD BEHAVIOURAL DEVELOPMENT: A PROSPECTIVE COHORT STUDY
Robinson M, Oddy WH, McLean NJ, Jacoby P, Pennell CE, de Klerk NH, Zubrick SR, Stanley FJ, Newnham JP.

- Full Study
- Crtitical Reviews and Responses

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Low–moderate prenatal alcohol exposure and risk to child behavioural development: a prospective cohort study

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Objective To examine the association of fetal alcohol exposure during pregnancy with child and adolescent behavioural development.

Design The Western Australian Pregnancy Cohort (Raine) Study recruited 2900 pregnancies (1989–91) and the 14-year follow up was conducted between 2003 and 2006.

Setting Tertiary obstetric hospital in Perth, Western Australia.

Population The women in the study provided data at 18 and 34 weeks of gestation on weekly alcohol intake: no drinking, occasional drinking (up to one standard drink per week), light drinking (2–6 standard drinks per week), moderate drinking (7–10 standard drinks per week), and heavy drinking (11 or more standard drinks per week).

Methods Longitudinal regression models were used to analyse the effect of prenatal alcohol exposure on Child Behaviour Checklist (CBCL) scores over 14 years, assessed by continuous *z*-scores and clinical cutoff points, after adjusting for confounders.

Main outcome measure Their children were followed up at ages 2, 5, 8, 10 and 14 years. The CBCL was used to measure child behaviour.

Results Light drinking and moderate drinking in the first 3 months of pregnancy were associated with child CBCL *z*-scores indicative of positive behaviour over 14 years after adjusting for maternal and sociodemographic characteristics. These changes in *z*-score indicated a clinically meaningful reduction in total, internalising and externalising behavioural problems across the 14 years of follow up.

Conclusions Our findings do not implicate light–moderate consumption of alcohol in pregnancy as a risk factor in the epidemiology of child behavioural problems.

Keywords Alcohol, behaviour, child behaviour checklist, prenatal exposures, Raine Study.

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Introduction

High levels of alcohol consumption during pregnancy have a teratogenic influence on fetal development, resulting in physical, cognitive and behavioural deficits.[1] The devastating impact of extreme levels of exposure to ethanol in pregnancy is evidenced in conditions such as fetal alcohol spectrum disorder and fetal alcohol syndrome.[1] Some studies claim that prenatal exposure to alcohol has a dose–response mechanism, where light drinking shows an effect mainly on behavioural and adaptive function and high levels are associated with more serious developmental impact and problems.[2] These data suggest that alcohol exposure at levels common in nonaddicted individuals, and so-called 'social drinking', may still be associated with long-term risk.[3] Many researchers have noted that most empirical enquiry into the effects of alcohol exposure during pregnancy has focused on and emphasised the devastating effects of high levels of alcohol exposure, often neglecting the influence of light–moderate drinking.[4]

The studies that have examined the effects of low levels of exposure to alcohol and behavioural development have failed to reach consensus, perhaps in part due to a number of methodological limitations.[5] For example, the reliability of retrospective data collected up to 17 years postpregnancy has been questioned.[5] Further, cutoff points used to categorise alcohol consumption (for example, 'low', 'medium' and 'high') have varied across studies,[6,7] and small sample sizes have hindered others.[8]

Maternal alcohol consumption of as little as one alcoholic drink per week has been associated with adverse child behavioural outcomes in a recent study;[7] however, this study placed virtually all alcohol consumption in one category (i.e. greater than or equal to one standard drink per week) so that very different patterns of consumption could not be distinguished within this group.[7] In addition, these results were seen only using clinical cutoff points for problem behaviours rather than across the range of scores, the results were limited to girls and the findings were only demonstrable with overall rather than syndrome-specific scores. Sood *et al.*[6] described alcohol intake in terms of fluid ounces of absolute alcohol consumed per day, and found that mothers who had a daily intake greater than or equal to 0.3 US fl. oz absolute alcohol had children with an increased risk of poor behaviour. Depending on country-specific norms, this amount equates to between half a standard drink and one and a half standard drinks per day;[9] therefore, this study also grouped women at the lower range of alcohol consumption with women who reported much higher patterns of consumption.[6]

Given that almost half of all pregnancies are not planned,[10] with many women consuming alcohol unaware that they are pregnant, alcohol exposure in the first trimester of pregnancy is likely to be common. It is important that women who are pregnant or contemplating becoming pregnant have access to advice on alcohol use that is based on solid empirical evidence. The aim of this study was to use a prospective pregnancy cohort to explore the relationship between alcohol intake that was concurrently assessed during pregnancy and subsequent child total, internalising and externalising behaviour.

Methods

Study design

The Western Australian Pregnancy Cohort (Raine) Study is a prospective longitudinal pregnancy cohort study of 2868 live births. Women were recruited into a randomised controlled trial to evaluate the effects of repeated ultrasound in pregnancy between May 1989 and November 1991 ($n = 2900$) through the public antenatal clinic at King Edward Memorial Hospital (KEMH) and nearby private clinics in Perth, Western Australia.[11] Comprehensive data regarding social and demographic characteristics were collected at 18 weeks of gestation, with further data collection at 34 weeks of gestation. Detailed clinical assessments were performed at birth and the study children and their families were followed up at 1, 2, 3, 5, 8, 10 and 14 years of age by questionnaire, which included sociodemographic and behavioural data (2, 5, 8, 10 and 14 years only).

Participants

Complete details of enrolment methods have been published elsewhere.[11] Briefly, to be eligible for enrolment, the women were required to have a pregnancy between 16 and 20 weeks of gestation (average 18 weeks), sufficient English language skills, an expectation to deliver at KEMH, and an intention to reside in Western Australia to allow for future follow up of their child. The potential for introducing bias by using a tertiary referral centre sample was minimised by enrolling women who booked before 18 weeks of gestation, which excluded those referred with complications.[12] Ninety percent of eligible women agreed to participate in the study and informed consent to participate in the study was obtained from the mother of each child at enrolment and at each subsequent follow up. The Human Ethics Committee at KEMH and/or Princess Margaret Hospital for Children approved all protocols for the study.

Loss to follow up

We achieved a reasonably low rate of attrition over 14 years, with 1860 of the original 2868 live births participating in the 14-year follow up (357 deferred from participating, 412 had withdrawn from the study, 207 were lost to follow up and 32 were deceased). The original cohort more closely reflected those women referred to a tertiary centre in over-representing socially disadvantaged families; however, those who were socially disadvantaged were less likely to remain in the study in the early years.[13] The characteristics of those who participated in the 14-year follow up compared with those who did not participate in the 14-year follow up are presented in Table 1. The selective attrition resulted in the sociodemographic characteristics of the study families participating in the 14-year follow up being equivalent to the characteristics of the general Western Australian population.[14]

Outcome variables

Child behaviour

The Child Behaviour Checklist for Ages 2–3 (CBCL/2-3), a 99-item, empirically validated measure of child behaviour by parent report,[15] was used at the 2-year follow up. At further follow ups the 118-item CBCL for Ages 4–18 (CBCL/4-18) was administered.[16] The CBCL demonstrated good sensitivity (83% overall) and specificity (67% overall)

Table 1. Characteristics of participants in the 14-year follow up (who completed the CBCL) compared with nonparticipants in the 14-year follow up (missing data not shown, column percentages presented)

	Non-participants (*n* = 1124) %	Participants (*n* = 1744) %	*P*-value
Alcohol intake 18 weeks			
No drinking	59.3	51.5	0.028
Occasional drinking	20.0	25.5	
Light drinking	15.4	19.4	
Moderate drinking	3.3	2.1	
Heavy drinking	2.0	1.6	
Maternal age at conception			
<20 years	15.0	6.8	<0.001
20–24.9 years	25.6	18.9	
25–29.9 years	30.1	30.5	
30–34.9 years	21.1	28.1	
35+ years	8.3	15.7	
Maternal education at pregnancy			
<High school completion	74.1	59.6	<0.001
High school completion	25.9	40.4	
Father living with family			
Yes	82.5	90.1	<0.001
No	17.5	9.9	
Low family income in pregnancy			
≤$24 000 per annum	41.9	25.6	<0.001
>$24 000 per annum	58.1	74.4	
Smoking in pregnancy			
None	65.6	77.5	<0.001
1–5 daily	9.6	7.9	
6–10 daily	9.6	5.3	
11–15 daily	7.0	4.5	
16–20 daily	4.9	3.2	
21+ daily	3.3	1.5	
Stress events in pregnancy			
None	20.4	22.9	0.005
1–2 events	38.3	42.2	
3+ events	41.2	34.9	
Year 2 behavioural problems			
Total	13.5	10.8	0.056
Internalising	10.1	8.0	0.077
Externalising	14.4	12.8	0.193
Year 5 behavioural problems			
Total	24.3	20.3	0.032
Internalising	19.0	17.7	0.264
Externalising	23.1	19.4	0.041
Year 8 behavioural problems			
Total	21.0	18.8	0.162
Internalising	19.2	19.4	0.489
Externalising	21.0	17.3	0.043
Year 10 behavioural problems			
Total	18.1	14.4	0.051
Internalising	18.7	17.4	0.310
Externalising	14.9	12.1	0.093
	Non-participants Mean (SD)	**Participants Mean (SD)**	***P*-value**
Gestational age (weeks)	38.69 (2.12)	38.82 (2.15)	0.104
Birthweight (g)	3283 (576)	3333 (591)	0.030

to a clinical psychiatric diagnosis and good test–retest reliability in a Western Australian clinical calibration.[17]

Both CBCL instruments produce a raw score that was transformed into three summary *z*-scores for a) total behaviour, b) internalising (withdrawal, somatic complaints, anxious/depressed) behaviour, and c) externalising (delinquency, aggression) behaviour. The *z*-scores for total, internalising and externalising behaviour were used as continuous scores in this study, with higher scores reflecting more disturbed emotions and behaviours. The raw scores produced by the CBCL were also converted into *T*-scores (standardised by age and sex) for total, internalising and externalising behaviour.[16] The recommended clinical cutoff scores ($T \geq 60$) were applied to the CBCL *T*-scores, to obtain three binary variables indicative of clinically significant total, internalising and externalising problems.[16] By the term 'clinically significant', we are referring to maladaptive behaviour that falls within a defined clinical range for behavioural problems.[16]

Predictor variables

Alcohol

Participants were requested at 18 weeks of gestation to provide an estimate of the total number of drinks consumed per week in the first 3 months of pregnancy. They were asked again at 34 weeks of gestation to provide an estimate of how much they were currently drinking. Participants were informed that the information was being collected for research only and would not be used in any way to make judgements about individuals' behaviour. Participants were asked to indicate the number of a) glasses of wine, b) nips of spirits, c) cans or 375-ml bottles of full-strength beer, and d) cans or 375-ml bottles of low-alcohol beer. These data were converted into a continuous variable representing the total number of standard drinks per week, and from there we used a categorisation of five levels: no drinking; occasional drinking (up to one standard drink per week); light drinking (2–6 standard drinks per week); moderate drinking (7–10 standard drinks per week); and heavy drinking (11 or more standard drinks per week). One standard drink was equivalent to 10 g of absolute alcohol.[18] Given that there were no quantified safe levels of drinking during pregnancy at the time, the categorisations used were based on other recent work in the area[19] and guidelines for alcohol consumption for nonpregnant women at the time.[18]

Control variables

The control variables for adjustment in our analyses included numerous prenatal and perinatal factors known to have some relationship with prenatal alcohol intake and mental health outcomes in children. These variables included maternal sociodemographic information from the prenatal period as follows: maternal age, maternal education, family income, the presence of the biological father in the family home, and maternal experience of stressful events in pregnancy.[20] Maternal smoking during pregnancy (cigarettes per day) was included in the model, as was the child's age at each follow up. The General Functioning Scale from the McMaster Family Assessment Device was applied to measure family functioning at each follow up except at age 2 years (when data were not available).[21]

Statistical analyses

Frequency distributions were compared for all outcome, predictor and control variables and cross-tabulations determined the relationships between the outcome and predictor variables. We used a linear regression model with a random intercept (random effects model) to examine the ability of our predictor variables to effect changes on the continuous CBCL *z*-score and generalised estimating equations (GEE; a random effect logistic regression model) to assess whether such changes in score reflected clinically meaningful differences in child behavioural problems (i.e. CBCL ≥ 60). Both models account for repeated observations of the same individuals over time. Firstly, the predictor variables were included in the random effects model and analysed using continuous CBCL *z*-scores for total, internalising and externalising behaviour at each year as outcomes. We followed this analysis with the inclusion of all control variables into the model for multivariable analysis. We examined family functioning as a potential mediator of the relationship between alcohol intake in pregnancy and later behavioural outcomes but it did not alter our results and therefore it was left out of the final model. The interaction between alcohol consumption and the child's age (years) was examined to look for associations between consumption and trajectories of CBCL scores; however, this was not significant. To examine the association between the predictor variables and clinically significant *T*-scores (binary indicator), we included the predictor and the control variables into GEE models with an unstructured working correlation matrix specification. This provided the best goodness-of-fit compared with other correlation structures to estimate the prevalence of child behaviour problems over time using odds ratios (OR). We accounted for nonlinear dependence of behaviour problems on age by adjusting for age and age-squared in the multivariable model. SPSS 15.0 (Chicago, IL, USA) was used for the analyses.

Results

A total of 2370 children contributed some data to the follow-up analyses. There was good consistency between

alcohol intake reported at 18 and 34 weeks of gestation, with the majority either remaining the same or reducing their intake (Table 2). The percentage of children with behavioural problems at each follow up was reasonably consistent across all groups of maternal alcohol intake at 18 weeks (Table 3). Higher alcohol intake in the first 3 months of pregnancy was significantly associated with an older maternal age, the absence of the biological father in the family home and increased smoking in pregnancy ($P < 0.001$) (Table 4). Maternal education and family income at 18 weeks of gestation did not show significant associations with increasing intake of alcohol in pregnancy, and the total number of stress events in pregnancy also showed no significant trend in relation to alcohol intake.

Alcohol intake and CBCL *z*-scores

We examined the mean difference in CBCL *z*-scores according to maternal alcohol intake status compared with the children of women who did not drink at all. In the unadjusted analysis, the children of mothers who consumed alcohol in the first 3 months of pregnancy were not significantly different from those born to mothers who did not drink alcohol in terms of behavioural development (Table 5). Although not significant in the unadjusted model, the direction of effect showed decreasing CBCL total, internalising and externalising *z*-scores for the children of mothers who reported consuming up to ten standard drinks per week at 18 weeks of gestation, representing better behaviour, while heavy drinking was associated with increased CBCL scores, representing poorer behaviour. Following adjustment for confounders, mothers who were light drinkers (2–6 standard drinks per week) in the first 3 months of gestation had children with significantly lower total and internalising *z*-scores across the 14 years of data collection compared with those who did not consume alcohol in the first months of pregnancy. The size of the effect increased following the adjustment for confounders in each of those alcohol consumption categories.

Prior to the adjustment for confounders, mothers who were light drinkers in pregnancy at 34 weeks of gestation had children with significantly lower total CBCL *z*-scores, but this result was not significant after adjustment, and there were no other associations between CBCL scores and alcohol consumption at 34 weeks of gestation with the exception of occasional drinking, which was significantly associated with higher total and externalising behaviour scores. The direction of risk in the adjusted model showed decreasing CBCL scores associated with light and moderate drinking. The interaction of age with alcohol consumption groups was not significant ($P = 0.2$), indicating that the difference in scores between groups was more or less the same at all ages.

Alcohol intake and CBCL behavioural problems

The CBCL problem data for the four drinking groups were compared (using odds ratios) with CBCL problems for the children of mothers who did not drink alcohol, and odds ratios <1 indicate that the group has fewer children reaching the clinical cutoff point than the nondrinking baseline group. The children of mothers who were light drinkers in the first 3 months of pregnancy had significantly fewer behavioural problems over the first 14 years of life than those whose mothers did not drink at all during pregnancy (Table 6). This effect was evident across all three domains in both the unadjusted and adjusted models. Drinking seven to ten standard drinks per week was also significantly associated with fewer total, internalising and externalising problems in the adjusted analyses, although the wider confidence intervals reflect the smaller numbers in this group. Once again, the direction of effect for the nonsignificant results (occasional drinking and heavy drinking) showed that alcohol intake in pregnancy was associated with fewer

Table 2. Comparison of reported alcohol intake group at 18 and 34 weeks of gestation*

	34-week data				
18-week data	**No alcohol (*n* = 1579) *n* (%)**	**Occ. drinking (*n* = 427) *n* (%)**	**Light drinking (*n* = 310) *n* (%)**	**Mod. drinking (*n* = 38) *n* (%)**	**Heavy drinking (*n* = 16) *n* (%)**
No alcohol (*n* = 1310) *n* (%)	1132 (86.4)	110 (8.4)	55 (4.2)	8 (0.6)	5 (0.4)
Occasional drinking (*n* = 539) *n* (%)	264 (49.0)	183 (34.0)	82 (15.2)	8 (1.5)	2 (0.4)
Light drinking (*n* = 419) *n* (%)	141 (33.7)	115 (27.4)	143 (34.1)	14 (3.3)	6 (1.4)
Moderate drinking (*n* = 60) *n* (%)	25 (41.7)	11 (18.3)	20 (33.3)	3 (5.0)	1 (1.7)
Heavy drinking (*n* = 42) *n* (%)	17 (40.5)	8 (19.0)	10 (23.8)	5 (11.9)	2 (4.8)

Kendall's tau-b = 0.44 (95% CI = 0.41, 0.47).
*Missing data not shown, row percentages presented.

behavioural problems in comparison with no alcohol intake in pregnancy in the first 3 months.

There were no significant relationships between any of the 34-week categories of alcohol intake and subsequent child behavioural problems between 2 and 14 years in the adjusted model. For light and moderate drinkers, the direction of effect was a reduction in problems; however, for heavy drinkers at 34 weeks of gestation, the multivariable results showed an increase in internalising and externalising problems compared with nondrinkers. Although not significant, occasional drinking at 34 weeks of gestation showed an association with increased problems across all three domains. The confidence intervals show a large range of effect, most likely because of the smaller sample sizes in the moderate and heavy categories.

Discussion

In this study we have shown that mothers who consumed light levels of alcohol (2–6 standard drinks per week) in the first 3 months of pregnancy had children with significantly lower total and internalising CBCL scores over 14 years, representing more positive behaviour, than nondrinkers at 3 months of gestation. These data also indicate that the children of light to moderate drinkers (2–10 standard drinks per week) were at a clinically meaningful lower risk of total, internalising and externalising behavioural problems than the children of women who did not drink.

Previous studies have suggested that drinking early in pregnancy was found to be associated with the highest risk of poor developmental outcomes for offspring when compared with alcohol intake later in pregnancy;[2] however, our results suggest that low–moderate alcohol intake early in pregnancy is not associated with poor behavioural outcomes for children. These data support other recent data that show low levels of alcohol exposure may not be associated with developmental risks.[19] Some studies that have suggested that low levels of alcohol intake may be a risk factor for poor behavioural outcomes have also included acknowledgements that across multiple domains of behaviour there are few significant results.[2,22] In studies where lower levels of alcohol consumption have been associated with increased risk, adjustment for relevant covariates has often diminished the strength of this effect.[23] Further, the complexity of alcohol consumption over time in quantity and pattern makes it very difficult to speculate as to safe levels of alcohol consumption and this may have led authors to err on the side of caution.[4] Our finding that heavy alcohol consumption was not significantly associated with poorer behavioural outcomes was unexpected. We suggest that this finding was influenced by the small number of heavy drinkers in this cohort.

Table 3. Percentage of participants with total, internalising (int) and externalising (ext) behavioural problems at each follow up according to their mother's alcohol intake at 18 weeks of gestation*

	Year 2 problems *n* (%) (*n* = 1952)			Year 5 problems *n* (%) (*n* = 2127)			Year 8 problems *n* (%) (*n* = 2037)			Year 10 problems *n* (%) (*n* = 1977)			Year 14 problems *n* (%) (*n* = 1744)		
	Total	Int	Ext	Total	Int	Ext	Total	Int	Ext	Total	Int	Ext	Total	Int	Ext
No alcohol *n* (%)	117 (11.3)	96 (9.3)	126 (12.2)	252 (22.6)	207 (18.6)	234 (21.0)	214 (20.0)	207 (19.3)	212 (19.9)	183 (17.8)	214 (20.8)	142 (13.8)	145 (16.2)	127 (14.2)	159 (17.7)
Occasional drinking *n* (%)	66 (13.6)	39 (8.1)	80 (16.5)	97 (18.5)	89 (17.0)	99 (18.9)	90 (18.2)	98 (19.8)	76 (15.4)	65 (13.0)	78 (15.6)	58 (11.6)	56 (12.6)	55 (12.4)	58 (13.1)
Light drinking *n* (%)	33 (9.3)	26 (7.4)	41 (11.6)	76 (19.1)	67 (16.8)	75 (18.8)	72 (18.6)	72 (18.6)	64 (16.5)	42 (11.3)	47 (12.6)	40 (10.8)	39 (11.5)	32 (9.5)	45 (13.3)
Moderate drinking *n* (%)	6 (10.9)	5 (9.1)	7 (12.7)	17 (29.8)	12 (21.1)	13 (22.8)	7 (13.5)	8 (15.4)	6 (11.5)	3 (5.9)	5 (9.8)	4 (7.8)	2 (5.6)	2 (5.6)	5 (13.9)
Heavy drinking *n* (%)	3 (12.0)	1 (4.0)	5 (20.0)	10 (31.3)	8 (25.0)	11 (34.4)	9 (29.0)	9 (29.0)	10 (32.3)	5 (19.2)	5 (19.2)	5 (19.2)	3 (10.7)	4 (14.3)	4 (14.3)

*Percentages represent those participants with behavioural problems compared with those without behavioural problems at each follow up.

Table 4. Frequency data for alcohol intake pattern reported at 18 weeks of gestation and control variables (n = 2370)*

	Alcohol in pregnancy					*P*-value
	No alcohol %	Occ. drinking %	Light drinking %	Moderate drinking %	Heavy drinking %	
Maternal age at conception						
<20 years	11.5	6.9	7.6	10.0	11.9	<0.001
20–24.9 years	23.5	18.2	16.7	13.3	14.3	
25–29.9 years	30.2	32.9	28.6	26.7	28.6	
30–34.9 years	23.7	26.8	29.4	28.3	40.5	
35+ years	11.0	15.2	17.7	21.7	4.8	
Maternal education at pregnancy						
<High school completion	67.0	59.3	61.1	66.7	71.4	0.099
High school completion	33.0	40.7	38.9	33.3	28.6	
Father living with family						
Yes	89.8	87.2	84.5	68.3	85.7	<0.001
No	10.2	12.8	15.5	31.7	14.3	
Low family income in pregnancy						
≤$24 000 per annum	32.8	28.4	28.9	29.8	32.5	0.163
>$24 000 per annum	67.2	71.6	71.1	70.2	67.5	
Smoking in pregnancy						
None	78.0	74.6	64.4	55.0	47.6	<0.001
1–5 daily	7.4	8.7	10.5	16.7	14.3	
6–10 daily	6.3	5.8	7.9	8.3	9.5	
11–15 daily	4.2	5.4	8.8	13.3	4.8	
16–20 daily	2.4	3.5	5.7	1.7	11.9	
21+ daily	1.8	2.0	2.6	5.0	11.9	
Stress events in pregnancy						
None	21.8	21.0	25.2	13.3	21.4	0.364
1–2 events	42.4	41.1	36.7	45.0	33.3	
3+ events	35.7	37.9	38.1	41.7	45.2	

*Missing data not shown, column percentages for each variable presented.

One of the strengths of this study was the longitudinal design that allowed for assessment of behavioural development at multiple time-points in the developmental trajectory through childhood and into adolescence. A prospective pregnancy cohort is essential for research of this nature to be unaffected by retrospective recall. Any study that intends to examine the effect of the prenatal environment on later behavioural outcomes needs to give careful consideration to the impact of a range of sociodemographic and family characteristics that could confound this effect. We were able to measure and adjust for a range of variables with the potential to influence behavioural outcomes. The administration of the CBCL at each of the follow ups is also a study strength because it is a well-validated behavioural assessment instrument with good internal consistency in the diagnosis of psychopathology.[24] We were able to avoid the problem of dichotomised predictors used in some studies that have the potential to hide dose–response patterns and threshold values (although the categorisation of predictor variables does retain the potential for some level of measurement error),[5] our study had adequate statistical power, and we used a tertiary maternity hospital catchment cohort rather than clinical samples as in previous studies.[25]

We used maternal self-report data for alcohol intake, as have the majority of studies on alcohol consumption and health outcomes.[22] We took steps to reassure the participants that they would not be judged on the information they provided on their drinking habits. Further, self-reported alcohol consumption data for the first trimester, where most results were observed, is likely to be more accurate than data collected later in pregnancy.[22] If there were self-report biases or issues with accurate retrospective recall for the first months of pregnancy at the 18-week assessment in this study, the alcohol consumption may be higher than reported, which could further strengthen our results. A limitation of the study was that our data could not reliably reflect the presence of binge drinking, given that the consumption of drinks per week at each time point was averaged, and patterns of

Table 5. Relationship between alcohol in pregnancy and CBCL *z*-scores [*n* (surveys) = 8531]*

Predictor variables	Linear random effects model—years 2 to 14 inclusive					
	Estimate of effects, 95% confidence interval, significance (*P*-value)					
	Unadjusted analysis			Adjusted analysis**		
	Total behaviour	Internalising behaviour	Externalising behaviour	Total behaviour	Internalising behaviour	Externalising behaviour
Alcohol 18 weeks†						
Occasional drinking	−0.05	−0.06	−0.03	−0.03	−0.05	−0.01
(≤1 drink per week)	−0.13, 0.03	−0.14, 0.01	−0.11, 0.05	−0.12, 0.07	−0.14, 0.04	−0.11, 0.08
n (women) = 539	0.238	0.101	0.441	0.581	0.267	0.788
Light drinking	−0.06	−0.04	−0.06	−0.12***	−0.11***	−0.10
(2–6 drinks per week)	−0.15, 0.03	−0.13, 0.04	−0.15, 0.03	−0.23, −0.01	−0.21, −0.00	−0.21, 0.01
n (women) = 419	0.195	0.319	0.174	0.031	0.044	0.064
Moderate drinking	−0.08	−0.11	−0.01	−0.27	−0.25	−0.20
(7–10 drinks per week)	−0.29, 0.13	−0.31, 0.09	−0.22, 0.20	−0.55, 0.00	−0.52, 0.02	0.48, 0.08
n (women) = 60	0.464	0.288	0.934	0.053	0.066	0.153
Heavy drinking	0.08	0.00	0.22	−0.04	−0.04	0.05
(11+ drinks per week)	0.20, 0.35	−0.26, 0.26	−0.05, 0.50	−0.36, 0.28	−0.35, 0.27	−0.27, 0.37
n (women) = 42	0.580	0.990	0.112	0.811	0.809	0.751
Alcohol 34 weeks						
Occasional drinking	−0.04	−0.04	−0.04	0.10***	0.06	0.14***
(≤1 drink per week)	−0.13, 0.05	0.13, 0.04	−0.13, 0.05	0.00, 0.21	−0.04, 0.16	0.04, 0.24
n (women) = 427	0.419	0.316	0.425	0.047	0.206	0.008
Light drinking	−0.11***	−0.10	−0.11	−0.05	−0.04	−0.03
(2–6 drinks per week)	−0.22, −0.01	−0.20, 0.00	−0.21, −0.00	−0.17, 0.07	−0.16, 0.07	−0.16, 0.09
n (women) = 310	0.039	0.050	0.050	0.432	0.464	0.575
Moderate drinking	−0.24	−0.23	−0.24	−0.21	−0.17	−0.18
(7–10 drinks per week)	−0.52, 0.04	−0.49, 0.04	−0.51, 0.04	−0.53, 0.11	−0.47, 0.14	−0.50, 0.14
n (women) = 38	0.098	0.090	0.097	0.199	0.294	0.270
Heavy drinking	0.06	−0.02	0.15	0.15	0.12	0.17
(11+ drinks per week)	−0.38, 0.51	−0.44, 0.40	−0.29, 0.59	−0.34, 0.63	−0.35, 0.59	−0.31, 0.66
n (women) = 16	0.790	0.925	0.498	0.557	0.621	0.488

*Number of surveys varied from one to five according to participation in the follow ups.
**Adjusted for maternal age, maternal education, presence of the biological father in the family home, family income, stress in pregnancy, maternal cigarette smoking, and child's age as a random slope.
***$P < 0.05$.
†Reflects drinking patterns in first 3 months of pregnancy, difference from *z*-score for no alcohol.

drinking may be relevant to assessing the influence of alcohol in pregnancy;[26] however, arbitrary definitions of binge patterns used in previous studies (for example, at least four drinks per day compared with fewer than four drinks per day)[26] do not necessarily capture the nature or effect of a binge drinking episode and should be interpreted with caution. We were unable to control for paternal alcohol intake in this study, which has been shown in other studies to moderate the association between intrauterine exposure to alcohol and child IQ.[27] As with any study of this nature it is important to consider that because of the large number of statistical tests performed, some of the significant findings reported may be due to chance. Our results may potentially be influenced by selective attrition given that those who were socially disadvantaged were less likely to remain in the cohort to age 14 years; however, a recent study using a similar cohort found that selective attrition had a minor influence on child behavioural outcomes.[28] Finally, alcohol consumption in pregnancy may be more common in women who experience mental distress in pregnancy[29] and although we were unable to adjust specifically for maternal psychopathology, we were able to control for the mothers' experience of stress, which is a good indicator of psychosocial distress.[30]

Table 6. Relationship between alcohol in pregnancy and CBCL problems ($T \geq 60$) at each age [n (surveys) = 8531]*

Predictor variables	Multivariate logistic GEE model–years 2 to 14 inclusive**					
	Odds ratio (OR), 95% confidence interval, significance (P-value)					
	Unadjusted analysis			Adjusted analysis****		
	Total behaviour	Internalising behaviour	Externalising behaviour	Total behaviour	Internalising behaviour	Externalising behaviour
Alcohol 18 weeks* **						
Occasional drinking	0.86	0.88	0.91	0.82	0.85	0.76*****
(≤1 drink per week)	0.71, 1.05	0.73, 1.06	0.75, 1.11	0.63, 1.06	0.67, 1.07	0.59, 0.99
n (women) = 539	0.140	0.171	0.351	0.133	0.164	0.042
Light drinking	0.77*****	0.80*****	0.80*****	0.63******	0.57******	0.69******
(2–6 drinks per week)	0.62, 0.96	0.65, 0.98	0.65, 1.00	0.46, 0.86	0.42, 0.76	0.51, 0.93
n (women) = 419	0.018	0.034	0.044	0.003	<0.001	0.014
Moderate drinking	0.80	0.75	0.86	0.43*****	0.31*****	0.46*****
(7–10 drinks per week)	0.50, 1.30	0.48, 1.18	0.52, 1.40	0.21, 0.88	0.14, 0.69	0.22, 1.00
n (women) = 60	0.375	0.209	0.535	0.020	0.004	0.049
Heavy drinking	1.14	1.12	1.38	0.68	0.76	0.97
(11+ drinks per week)	0.71, 1.82	0.67, 1.89	0.82, 2.33	0.31, 1.47	0.33, 1.76	0.49, 1.93
n (women) = 42	0.592	0.661	0.222	0.323	0.519	0.931
Alcohol 34 weeks†						
Occasional drinking	0.85	0.89	0.81	1.24	1.06	1.22
(≤1 drink per week)	0.68, 1.06	0.73, 1.09	0.65, 1.01	0.93, 1.65	0.82, 1.37	0.92, 1.62
n (women) = 427	0.141	0.273	0.057	0.137	0.683	0.168
Light drinking	0.75*****	0.81	0.74*****	0.88	0.86	0.77
(2–6 drinks per week)	0.59, 0.97	0.63, 1.03	0.57, 0.95	0.63, 1.23	0.61, 1.20	0.56, 1.05
n (women) = 310	0.029	0.087	0.019	0.460	0.378	0.099
Moderate drinking	0.72	0.52	0.79	0.48	0.49	0.53
(7–10 drinks per week)	0.36, 1.44	0.24, 1.11	0.39, 1.61	0.20, 1.14	0.16, 1.49	0.19, 1.44
n (women) = 38	0.355	0.089	0.520	0.098	0.207	0.210
Heavy drinking	1.29	0.80	1.35	1.19	1.21	1.24
(11+ drinks per week)	0.56, 2.96	0.37, 1.74	0.61, 3.00	0.30, 4.68	0.49, 2.95	0.40, 3.86
n (women) = 16	0.551	0.576	0.466	0.802	0.683	0.713

*Number of surveys varied from one to five according to participation in the follow ups.
**Obtained with binomial distribution, logit link and unstructured working correlation matrix.
***Reflects drinking patterns in first 3 months of pregnancy, reference category no alcohol.
****Adjusted for maternal age, maternal education, presence of the biological father in the family home, family income, stress in pregnancy, child's age at follow up (and child's age at follow-up squared), and maternal cigarette smoking.
*****$P < 0.05$, ******$P < 0.005$.
†Reference category no alcohol.

Possible mechanisms

Our findings could be explained in part by the psychosocial characteristics of mothers who drink in moderation during early pregnancy: more specifically, the characteristics that make these mothers different from mothers who do not drink at all. Substance-use research suggests that moderate drinkers are mentally healthier than both abstainers and addicts,[31] which is attributed to the self-efficacy and behavioural self-management required for moderating substance intake.[32,33] The self-control that allows light–moderate drinkers to contain and manage their drinking quite plausibly enables better parenting and positive child well-being.[34] Numerous socioeconomic and medical factors may also confound the differences between moderate drinkers and abstainers,[35] and our finding that maternal education and family income were not associated with alcohol intake indicates that drinking habits are not easily predicted by measurable sociodemographic variables.

We propose that biological mechanisms may also help to explain the results we have observed in this study. Alcohol is easily distributed from the maternal bloodstream to the fetus,[25] and alcohol may affect hypothalamic–pituitary–adrenal axis reactivity which is linked to neonatal behaviour and the development of psychopathology.[25] Given that

maternal prenatal anxiety is a risk for the development of behavioural problems in childhood,[36] low doses of alcohol may have a moderating effect on maternal mood.[32] Further, when considering the biological mechanisms through which a light intake of alcohol in pregnancy may reduce the incidence of child behavioural problems, it is useful to examine the broader literature on alcohol and population health. Increasing alcohol intake is generally found to show a *U*-shaped or *J*-shaped curve in relation to physical health outcomes, for example increased intake of alcohol is thought to be protective against cardiovascular mortality up to a threshold point.[37,38] The recommended quantity of alcohol consumption for women to protect against cardiovascular mortality is one or two drinks daily for 5–6 days a week,[39] and although these findings are not within the context of pregnancy, they are similar amounts to the levels that we found to be associated with a reduction in child behavioural problems. Recent studies also suggest the potential for specific genetic variants to moderate the relationship between maternal cigarette smoking during pregnancy and child behaviour and it is yet to be seen what influence genetic factors may have over the relationship between alcohol intake during pregnancy and child behavioural outcomes.[40–42]

Implications of these findings

The antenatal period is one where women are often advised to give up behaviours that they may have previously enjoyed, including alcohol, smoking, high-fat foods and caffeine.[43] Therefore, enhancing the social and medical supports for those who find this lifestyle change difficult is important. We believe that these findings are important for the community in relation to limiting the overestimation of risk that accompanies emotive subjects such as teratogenic exposure in pregnancy. With up to 50% of pregnancies unplanned, the first 18 weeks of pregnancy are likely to encompass a period of time where the pregnancy is unknown or unconfirmed, and as such may be reflective of women's usual drinking patterns rather than an intentional change in drinking behaviour due to pregnancy. Women who believe their actions before discovering they are pregnant may have harmed their unborn child may experience guilt, anxiety and critical judgement from their peers. As previously mentioned, maternal antenatal anxiety and stress are known to increase the risk of child behavioural problems,[36] highlighting the need for understanding and the reservation of judgement. Given the guilt and anxiety that are associated with the consumption of alcohol during pregnancy it is important to acknowledge that alcohol consumption and behavioural consequences for the child do not necessarily follow a simple linear dose–response pattern. It should be noted that these results relate to low–moderate alcohol consumption and child behavioural outcomes only and there may be other cognitive and neurodevelopmental outcomes that relate to alcohol consumption in different ways.

Conclusion

Our findings, taken together with data from other recent studies, indicate that low levels of alcohol consumption by women in early pregnancy do not appear to be harmful to subsequent mental health of the offspring whereas high levels of alcohol exposure during pregnancy should be discouraged during pregnancy because there are consistent findings across multiple studies that high levels of alcohol exposure during pregnancy are associated with an increase in adverse outcomes for the offspring. Despite the fact that our analyses have controlled for socioeconomic status, the results of our study may still reflect other unmeasured psychosocial differences between women who drink small amounts of alcohol during pregnancy and those who are abstainers, and future studies addressing this issue require a very careful assessment of maternal and paternal alcohol consumption and sociodemographic factors. Our data suggest that women who conceive unexpectedly while consuming limited amounts of alcohol have not placed their unborn child at increased risk of behavioural problems during childhood.

Disclosure of interest

All authors declare that there are no conflicts of interest to disclose.

Contribution to authorship

The contributions of individual authors to this paper are as follows: planning research (Monique Robinson, Craig Pennell, Nicholas de Klerk, Fiona Stanley, John Newnham); executing research (Monique Robinson, Wendy Oddy, Neil McLean, Peter Jacoby, Craig Pennell, Nicholas de Klerk, John Newnham); analysing data (Monique Robinson, Peter Jacoby, Nicholas de Klerk); interpreting data (Monique Robinson, Wendy Oddy, Neil McLean, Peter Jacoby, Craig Pennell, Nicholas de Klerk, Stephen Zubrick, Fiona Stanley, John Newnham); and writing (Monique Robinson, Wendy Oddy, Neil McLean, Peter Jacoby, Craig Pennell, Nicholas de Klerk, John Newnham).

Details of ethics approval

The Human Ethics Committee at KEMH approved the protocols for this study on 18 May 1989. Princess Margaret Hospital for Children approved all subsequent protocols for the study, with the first approval being granted on 23 August 1990 under the reference code RE90-23.4 and the most recent approval for the 14-year follow up granted on 20 March 2003 under the reference code EC03-14.7.

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References

1 O'Leary CM. Fetal alcohol syndrome: diagnosis, epidemiology, and developmental outcomes. *J Paediatr Child Health* 2004;40:2–7.
2 Olson HC, Streissguth AP, Sampson PD, Barr HM, Bookstein FL, Thiede K. Association of prenatal alcohol exposure with behavioral and learning problems in early adolescence. *J Am Acad Child Adolesc Psychiatry* 1997;36:1187–94.
3 Williams J, Ross L. Consequences of prenatal toxin exposure for mental health in children and adolescents. *Eur Child Adolesc Psychiatry* 2007;16:243–53.
4 Sampson PD, Streissguth AP, Bookstein FL, Barr HM. On categorizations in analyses of alcohol teratogenesis. *Environ Health Perspect* 2000;108(Suppl 3):421–8.
5 Linnet KM, Dalsgaard S, Obel C, Wisborg K, Henriksen TB, Rodriguez A, *et al.* Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. *Am J Psychiatry* 2003;160:1028–40.
6 Sood B, Delaney-Black V, Covington C, Nordstrom-Klee B, Ager J, templin T, *et al.* Prenatal alcohol exposure and childhood behavior at age 6 to 7 years: I. dose-response effect. *Pediatrics* 2001;108:E34.
7 Sayal K, Heron J, Golding J, Emond A. Prenatal alcohol exposure and gender differences in childhood mental health problems: a longitudinal population-based study. *Pediatrics* 2007;119:E426–34.
8 Johnson CH, Vicary JR, Heist CL, Corneal DA. Moderate alcohol and tobacco use during pregnancy and child behavior outcomes. *J Prim Prev* 2001;21:367–79.
9 Turner C. How much alcohol is in a 'standard drink'? An analysis of 125 studies *Addiction* 1990;85:1171–5.
10 Colvin L, Payne J, Parsons D, Kurinczuk JJ, Bower C. Alcohol consumption during pregnancy in nonindigenous West Australian women. *Alcohol Clin Exp Res* 2007;31:276–84.
11 Newnham JP, Evans SF, Michael CA, Stanley FJ, Landau LI. Effects of frequent ultrasound during pregnancy: a randomised controlled trial. *Lancet* 1993;342:887–91.
12 Williams L, Evans SF, Newnham JP. Prospective cohort study of factors influencing the relative weights of the placenta and the newborn infant. *BMJ* 1997;314:1864–8.
13 Li J, Kendall GE, Henderson S, Downie J, Landsborough L, Oddy WH. Maternal psychosocial wellbeing in pregnancy and breastfeeding duration. *Acta Paediatr* 2008;97:221–5.
14 Kendall GE. Children in families in communities: a modified conceptual framework and an analytic strategy for identifying patterns of factors associated with developmental health outcomes in childhood. PhD thesis, The University of Western Australia, 2003.
15 Achenbach TM, Edelbrock C, Howell CT. Empirically based assessment of the behavioural/emotional problems of 2- and 3-year-old children. *J Abnorm Child Psychol* 1987;15:629–50.
16 Achenbach TM. *Manual for the Child Behavior Checklist/4–18 and 1991 Profile*. Burlington: University of Vermont, Department of Psychiatry, 1991.
17 Zubrick S, Silburn S, Gurrin L, Teoh H, Shepherd C, Carlton J, *et al. Western Australian Child Health Survey: Education, Health and Competence*. Perth, Western Australia: Australian Bureau of Statistics and the Telethon Institute for Child Health Research (ISBN 0 642 17239 0); 1997.
18 Pols RG, Hawks DV. *Is there a safe level of daily consumption of alcohol for men and women? Recommendations regarding responsible drinking behaviour*. Canberra: National Health and Medical Research Council, Australian Government Publishing Service, 1987.
19 Kelly Y, Sacker A, Gray R, Kelly J, Wolke D, Quigley MA. Light drinking in pregnancy, a risk for behavioural problems and cognitive deficits at 3 years of age? *Int J Epidemiol* 2009;38:129–40.
20 Robinson M, Oddy WH, Li J, Kendall GE, de Klerk NH, Silbrun SR, *et al.* Pre- and postnatal influences on preschool mental health: a large-scale cohort study. *J Child Psychol Psychiatry* 2008;49:1118–28.
21 Epstein N, Baldwin L, Bishop D. The McMaster family assessment device. *J Marital Fam Ther* 1983;9:171–80.
22 Streissguth AP, Barr HM, Sampson PD, Bookstein FL. Prenatal alcohol and offspring development: the first fourteen years. *Drug Alcohol Depend* 1994;36:89–99.
23 Barr HM, Darby BL, Streissguth AP, Sampson PD. Prenatal exposure to alcohol, caffeine, tobacco, and aspirin – effects on fine and gross motor-performance in 4-year-old children. *Dev Psychol* 1990;26:339–48.
24 Warnick EM, Bracken MB, Kasl S. Screening efficiency of the child behavior checklist and strengths and difficulties questionnaire: a systematic review. *Child Adolesc Ment Health* 2008;13:140–7.
25 Huizink AC, Mulder EJ. Maternal smoking, drinking or cannabis use during pregnancy and neurobehavioral and cognitive functioning in human offspring. *Neurosci Biobehav Rev* 2006;30:24–41.
26 Sayal K, Heron J, Golding J, Alati R, Smith GD, Gray R, *et al.* Binge pattern of alcohol consumption during pregnancy and childhood mental health outcomes: longitudinal population-based study. *Pediatrics* 2009;123:e289–96.
27 Alati R, Macleod J, Hickman M, Sayal K, May M, Smith GD, *et al.* Intrauterine exposure to alcohol and tobacco use and childhood IQ: findings from a parental-offspring comparison within the Avon Longitudinal Study of Parents and Children. *Pediatr Res* 2008;64:659–66.
28 Wolke D, Waylen A, Samara M, Steer C, Goodman R, Ford T, *et al.* Selective drop-out in longitudinal studies and non-biased prediction of behaviour disorders. *Br J Psychiatry* 2009;195:249–56.
29 Ahluwalia IB, Mack KA, Mokdad A. Mental and physical distress and high-risk behaviors among reproductive-age women. *Obstet Gynecol* 2004;104:477–83.
30 Seguin L, Potvin L, St-Denis M, Loiselle J. Chronic stressors, social support, and depression during pregnancy. *Obstet Gynecol* 1995;85:583–9.

31 Stranges S, Notaro J, Freudenheim JL, Calogero RM, Muti P, Farinaro E, *et al.* Alcohol drinking pattern and subjective health in a population-based study. *Addiction* 2006;101:1265–76.

32 Peele S, Brodsky A. Exploring psychological benefits associated with moderate alcohol use: a necessary corrective to assessments of drinking outcomes? *Drug Alcohol Depend* 2000;60:221–47.

33 Vaillant GE. *The Natural History of Alcohol Revisited*. Cambridge, MA: Harvard University Press, 1995.

34 Finkenauer C, Engels R, Baumeister RF. Parenting behaviour and adolescent behavioural and emotional problems: the role of self-control. *Int J Behav Dev* 2005;29:58–69.

35 Lindberg ML, Amsterdam EA. Alcohol, wine and cardiovascular health. *Clin Cardiol* 2008;31:347–51.

36 O'Connor TG, Heron J, Golding J, Beveridge M, Glover V. Maternal antenatal anxiety and children's behavioural/emotional problems at 4 years: report from the Avon Longitudinal Study of Parents and Children. *Br J Psychiatry* 2002;180:502–8.

37 Newnham JP, Pennell CE, Lye SJ, Rampono J, Challis JRG. Early life origins of obesity. *Obstet Gynecol Clin North Am* 2009;36: 227–44.

38 Holman CD, English DR, Milne E, Winter MG. Meta-analysis of alcohol and all-cause mortality: a validation of NHMRC recommendations. *Med J Aust* 1996;164:141–5.

39 McElduff P, Dobson AJ. How much alcohol and how often? Population based case–control study of alcohol consumption and risk of a major coronary event *BMJ* 1997;314:1159–64.

40 Rice F, Harold GT, Boivin J, Hay DF, van den Bree M, Thapar A. Disentangling prenatal and inherited influences in humans with an experimental design. *Proc Natl Acad Sci U S A* 2009;106:2464–7.

41 Thapar A, Rice F, Hay D, Boivin J, Langley K, van den Bree M, *et al.* Prenatal smoking might not cause attention-deficit/hyperactivity disorder: evidence from a novel design. *Biol Psychiatry* 2009;66:722–7.

42 Freathy RM, Ring SM, Shields B, Galobardes B, Knight B, Weedon MN, *et al.* A common genetic variant in the 15q24 nicotinic acetylcholine receptor gene cluster (CHRNA5-CHRNA3-CHRNB4) is associated with a reduced ability of women to quit smoking in pregnancy. *Hum Mol Genet* 2009;18:2922–7.

43 Pirie PL, Lando H, Curry SJ, McBride CM, Grothaus LC. Tobacco, alcohol, and caffeine use and cessation in early pregnancy. *Am J Prev Med* 2000;18:54–61.

Commentary on 'Low–moderate prenatal alcohol exposure and the risk to child behavioural development: a prospective cohort study'

Excessive maternal alcohol consumption during pregnancy is associated with various severe growth and neurobehavioral consequences in the offspring (Jones *et al. Lancet* 1973;301:1267–71). More recently, studies have focused on the effects of low to moderate alcohol consumption, which commonly refers to less than one unit per day. Low to moderate levels of maternal alcohol consumption during pregnancy seem not to be consistently associated with fetal growth restriction or increased risks of birth complications (Jaddoe *et al. Ann Epidemiol* 2007;17:834–40, Bakker *et al. Int J Epidemiol* 2010: doi: 10.1093/ije/dyq047). However, exposure to low levels of alcohol during fetal life may still lead to neurodevelopmental maladaptations, without affecting early growth. Most studies suggesting associations between low maternal alcohol consumption during pregnancy and behavioural and cognitive outcomes in children were mainly based on small study samples and only took account of a limited number of covariates.

The article by Robinson *et al.* (*BJOG* 2010; doi: 10.1111/j.1471-0528.2010.02596.x) adds important information to this topic. They examined the associations of fetal alcohol exposure at the gestational ages of 18 and 34 weeks with child and adolescent behavioural development in a prospective cohort study. Childhood behavioural development was measured at the ages of 2, 5, 8, 10 and 14 years by means of the standardised and validated Child Behaviour Checklist questionnaire, which enables assessment of total, internalising and externalising problem behaviour. They did not observe any adverse effect of low to moderate alcohol consumption during pregnancy at either 18 or 34 weeks, on behavioural outcomes in childhood. Their findings suggest that light and moderate drinking in the first 3 months of pregnancy was associated with a reduction in total, internalising and externalising behavioural problems during childhood and adolescence. These results are in line with two recent large population-based cohort studies. A recent study among more than 20 000 children showed no association of low doses of maternal alcohol consumption during pregnancy with the risks of attention deficit and hyperreactivity disorder after adjustment for social adversity and smoking (Rodriguez *et al. J Child Psychol Psychiatry* 2009;50:1073–83). Similarly, results from the nationally representative prospective UK Millennium Cohort study showed no effects of low alcohol consumption during pregnancy on behavioural and cognitive outcomes in more than 9000 preschool children (Kelly *et al. Int J Epidemiol* 2009;38:129–40). Interestingly, like the study by Robinson *et al.*, results from this study suggested even a protective effect of low to moderate alcohol consumption for development of behavioural problems. Although several biological explanations for these associations have been proposed, residual confounding due to, for example, social and dietary circumstances, should be considered. In many contemporary Western populations, low to moderate alcohol consumption during pregnancy is common in socially advantaged, higher educated and healthier women.

Although current evidence from epidemiological studies does not strongly suggest that low to moderate maternal alcohol consumption during pregnancy adversely affects the health of their children, more information is needed on specific critical periods during fetal life and threshold levels above which alcohol consumption might have adverse effects. This information is needed for updating recommendations for safe low alcohol consumption during pregnancy.

Disclosure of interests

No conflict of interest. ■

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Commentary on 'Low–moderate prenatal alcohol exposure and risk to child behavioural development: a prospective cohort study'

Robinson *et al.* (*BJOG* 2010; doi: 10.1111/j.1471-0528.2010.02596.x) use data from the Western Australian Pregnancy Cohort to show that children exposed prenatally to low–moderate alcohol actually do better on the Child Behaviour Checklist (CBCL) than those born to mothers who abstain. This finding was unexpected and is inconsistent with a substantial body of evidence from large, prospective, longitudinal studies that have documented a broad range of adverse effects on growth, cognition and behaviour in children exposed at low-to-moderate levels using measures that are more sensitive than the CBCL (e.g. Day *et al. Alcohol Clin Exp Res* 2002;26:1584–91; Jacobson *et al. Alcohol Clin Exp Res* 2004;28:1732–45; Holmgren. Swedish National Institute of Public Health, 2009).

A major limitation of the Robinson *et al.* study is the use of abstainers as the reference control group. Light–moderate drinkers are often socioeconomically more advantaged than abstainers, and their children are, therefore, likely to exhibit more optimal behavioural outcomes (http://pubs.niaaa.nih.gov/publications/ModerateDrinking-03.htm, 2003; www.fasdsg.org/News_Publications.php?topic=1&category=1, 2008). Given that the abstainers' income and education are markedly lower compared with the occasional–light drinkers in the Robinson *et al.* study, combining the abstainers and occasional–light drinkers would have provided a more appropriate reference group.

The absence of significant adverse effects in the heavily exposed children also raises questions about the utility of the parental CBCL for detecting subtle effects in this population. To determine a threshold, one must first confirm the adverse effect on the outcome being examined and then determine the lowest dose at which the effect continues to be evident. The data from studies examining the CBCL in relation to prenatal alcohol exposure have been inconsistent (Mattson and Riley. *Alcohol Clin Exp Res* 2000;24:226–31). By contrast, teacher ratings on this instrument reliably detect adverse effects at low–moderate exposures (Jacobson *et al. J Pediatr* 2006;148:30–7).

In addition, the Robinson *et al.* data were not analysed to assess the effects of binge drinking (at least four drinks/occasion for women). Studies in animals and in humans have found that dose/occasion is often more important than mean amount of alcohol/week in determining adverse effects (Bonthius and West. *Teratology* 1991;44:147–63; Jacobson *et al. Alcohol Clin Exp Res* 1998;22:345–51). Most women do not drink daily but concentrate their drinking on 1 or 2 days/week, thereby exposing the fetus to levels found to be harmful, even when maternal average volume of alcohol/week is low (Jacobson and Jacobson. In Nelson CS, editor, *Minnesota Symposia on Child Psychology*. Mahwah, NJ: Lawrence Erlbaum; 2000).

Women who drink at low levels 'may experience [unwarranted] guilt, anxiety and critical judgement from their peers'. Nevertheless, it is not appropriate to reassure them or their health providers, based on the limited findings reported in this paper, that low–moderate doses of alcohol during pregnancy may be beneficial. Also, advice that low doses of alcohol in pregnancy could be beneficial may encourage drinking by pregnant women with a propensity for alcohol abuse who may not recognise when their drinking becomes excessive. In our research we have found evidence of substantial individual differences in vulnerability to the adverse effects of fetal alcohol exposure based on maternal age, alcohol abuse history and genetic make-up (Jacobson *et al.*, 2004, 2006 cited above). For this reason, even light drinking could put the fetus at risk where the mother or infant is particularly vulnerable. Although there is no

evidence that an occasional drink during pregnancy is consequential, abstaining from alcohol during pregnancy is still the best advice the obstetrician can offer.

Disclosure of interests

Neither of the authors have any conflicts of interest that would bias the commentary or interpretation of the findings presented here. ■

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